Volume 10, Number 1, January 1990
Jumada Al-Thani 1410

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ANNALS of Saudi Medicine

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Cough is a major protective mechanism which should only be suppressed if it is particularly troublesome, unproductive and not associated with an underlying treatable condition.[1] In such cases a simple preparation containing a single agent is often preferred. The problem is many antitussives today also contain one or more additional agents like caffeine, antihistamines, analgesics, decongestants, anticholinergics, expectorants or even vitamins – the so called cough cocktail. Most are either ineffective or contain inappropriate combinations which may be dangerous.[1]

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1. Holmes J Aust Prescriber 1987: 10(4): 62-65

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Vol. 10

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ANNALS OF SAUDI MEDICINE

Aims and Scope

The *Annals of Saudi Medicine* is a joint project of the King Faisal Specialist Hospital and Research Centre and the King Saud University College of Medicine and King Khalid University Hospital. The journal is typeset and printed at the King Saud University Press, Riyadh, Saudi Arabia. Since July 1985, the *Annals* has incorporated *The King Faisal Specialist Hospital Medical Journal*, established in 1980.

The *Annals* is a bimonthly multidisciplinary medical journal. High-quality papers, written in English, dealing with aspects of clinical, academic or investigative medicine or research will be welcome. Emphasis is placed on matters relating to medicine in Saudi Arabia in particular, and the Middle East in general, though articles are welcome from anywhere in the world, and the *Annals* has worldwide readership.

The *Annals* publishes original articles, case reports, letters to the editor, editorials, and from time to time, special communications, commentaries, and review articles. Abstracts of meetings and symposia sponsored by the Joint Board for Postgraduate Medical Education of Saudi Arabia are published, and the proceedings of such symposia may be published if the Editorial Board considers them appropriate and relevant. The Editorial Board wishes to minimize delay between manuscript submission, decision, and publication, and accordingly authors are requested to follow carefully the instructions set out under "Information for Authors."

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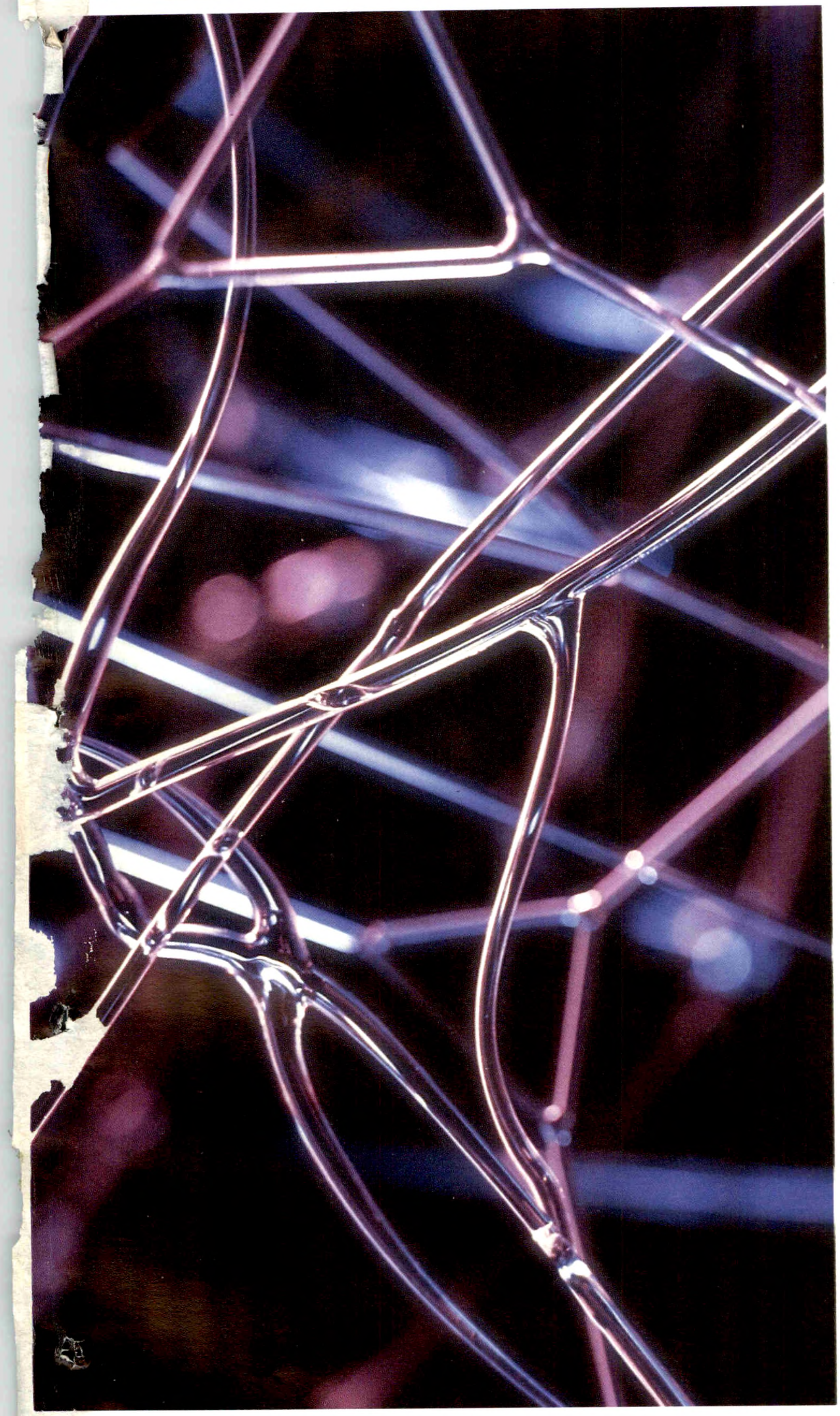
A BREAKTHROUGH IN CORONARY THROMBOLYSIS



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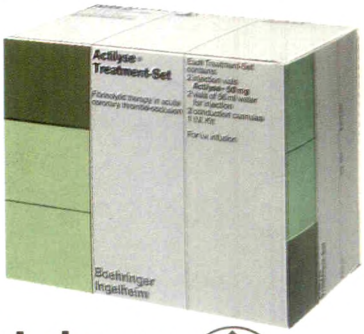
1. Van de Werf et al J Am Coll Cardiol 1988:12:14A-9A
2. TIMI Study Group N Engl J Med 1985:312 (14)932



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REFERENCES: 1. Roth SH, *Am J Med* 1987; **83** (Suppl 4B): 25–30. 2. Appelrouth DJ *et al*, *Am J Med* 1987; **83** (Suppl 4B): 78–81. 3. Carle WK, Rotman H, *R Soc Med Int Congr Symp Ser* 1985; (69): 139–148. 4. Brobyn RD, *Am J Med* 1987; **83** (Suppl 4B): 50–54.

RELIFEX is a product of research from Beecham Pharmaceuticals, Brentford, England. Further information is available from the company on request.

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على مرّ العُصُور ورافقت مختلف الحضارات
وأجمع العالم كلّه على اعتباره غذاءً
سليمًا طبيعيًّا يمنحُ القوّة والعافية .
نستله تُنتج الآن مزيجًا فريدًا من نوعِه
هو سيريلاك بالقمح والعسل ، فهو يجمع
بين ميّزات القمح وغذاء الحليب ومنافع العسل .
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Special formula for low birthweight infants
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NESTLÉ
Net weight 400 g

PRE-NAN is a special infant formula accurately adjusted to safely meet the needs of the low-birthweight infant. For normal enteral feeding or by naso-gastric tube, from the first days of life until a bodyweight of 4 to 5 kg is achieved.

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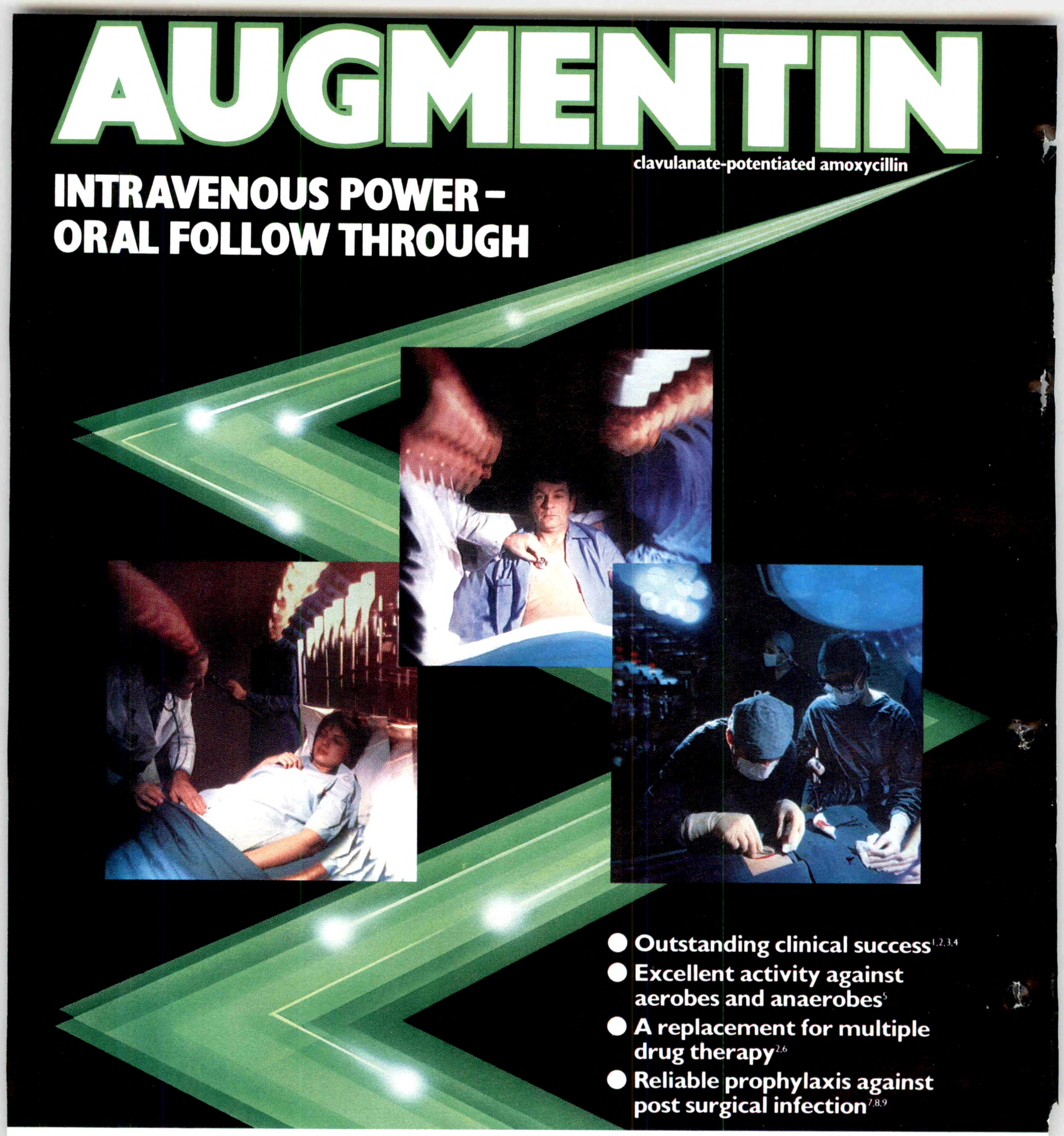
IMPORTANT NOTICE The World Health Organization (WHO*) has recommended that pregnant women and new mothers be informed of the benefits and superiority of breastfeeding – in particular the fact that it provides the best nutrition and protection from illness for babies. Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle-feeding or other foods and drinks should be discouraged since it will have a negative effect on breast-feeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breast-feed.

For most low birthweight infants the mother should be encouraged to express her breast-milk to feed her baby, if direct breast feeding is impossible. If breast-milk is not available, or must be supplemented, a special formula adapted to the specific nutritional needs of low birthweight infants should be used under strict medical control.

Continued use of a special formula should be assessed case by case in relation to the baby's progress, and bearing in mind any social and financial implications for the family. For example, if a baby is exclusively bottle-fed, more than one can (450 g) per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breast-milk is not only the best, but also the most economical food for babies. If a decision to use an infant formula is taken, it is important to give instruction on correct preparation methods, emphasizing that unboiled water, unboiled bottles or incorrect dilution can all lead to illness.

* See: International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981.



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- Excellent activity against aerobes and anaerobes[5]
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References 1. Excerpta Medica, **CCP4**, (1983), 207. 2. J. Antimicrob. Chemother., (1982) **10**, (1), 67. 3. Proc. 4th Mediterr. Congr. Chemother. Rhodes, (1985), **4**, (2 suppl.): 199. 4. Excerpta Medica, **ICS 544**, (1980), 277. 5. Ibid. (1980), 173. 6. Med. Int. (1983), (Suppl: Readings in Infections), 2. 7. Proc. 4th Mediterr. Congr. Chemother. Rhodes, (1985), **4**, (2 Suppl.), 776. 8. Br. J. Surg., (1985), **72**, (7), 571. 9. Proc. 26th ICAAC New Orleans, (1986), Abstr. 472.

Prescribing Information

Indications: Upper/lower respiratory tract infections: sinusitis, tonsillitis, otitis media, acute and chronic bronchitis, pneumonia, empyema, lung abscess. Skin and soft tissue infections: Boils/abscesses, cellulitis, wound infections, intra-abdominal sepsis. Genito-urinary tract infections: cystitis, urethritis, pyelonephritis, septic abortion, pelvic infections, chancroid, gonorrhoea. Osteomyelitis, septicaemia, peritonitis, surgical prophylaxis.

Oral dosage: Adults and children over 12 years: One tablet tds. Children 7-12 years: 10ml of 156mg syrup. Children 2-7 years: 5ml of 156mg syrup. Children 9 months-2 years: 2.5ml of 156mg syrup. Children below 9 months: No suitable presentation currently available. In severe infections the dosage may be doubled.

Intravenous dosage: Adults and children over 12 years 1.2g 6-8 hourly. Children 3 months-12 years 30mg/kg 6-8 hourly. Children below 3 months see pack insert leaflet. Surgical prophylaxis: Adults: 1.2g at induction of anaesthesia. Procedures longer than 1 hour require subsequent doses (up to 4 in 24 hours). Treatment with AUGMENTIN should not be extended beyond 14 days without review.

Contra-indication: Penicillin hypersensitivity. **Precautions:** A number of studies at high dosages have shown AUGMENTIN to be free from teratogenicity in animals; however its safety in human pregnancy has not yet been established. There is no experience of AUGMENTIN I.V. in human pregnancy therefore its use in pregnancy cannot be recommended. Changes in liver function tests have been observed in some patients receiving intravenous AUGMENTIN. The clinical significance of these changes is uncertain but AUGMENTIN should be used with care in patients with evidence of severe hepatic dysfunction. Dosage for patients with moderate or severe renal impairment should be adjusted as described in the pack insert leaflet. **Side-effects:** Uncommon, mainly mild and transitory eg. diarrhoea, indigestion, nausea, vomiting, candidiasis. If gastro-intestinal side-effects occur with oral therapy they may be reduced by taking AUGMENTIN at the start of meals. In the event of an urticarial or morbilliform rash discontinue treatment. Phlebitis at the site of injection has been reported.

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Storage and Stability: See pack insert leaflet.

Further information is available on request.
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Confidence

WHEN IMPAIRED HOST DEFENCES PUT PATIENTS AT RISK

Most hospitalised patients are to some degree immunocompromised and are therefore at special risk of infection.

Minor

- old age
- poor nutrition
- neonate
- catheters

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- chronic debilitating diseases
- intensive care

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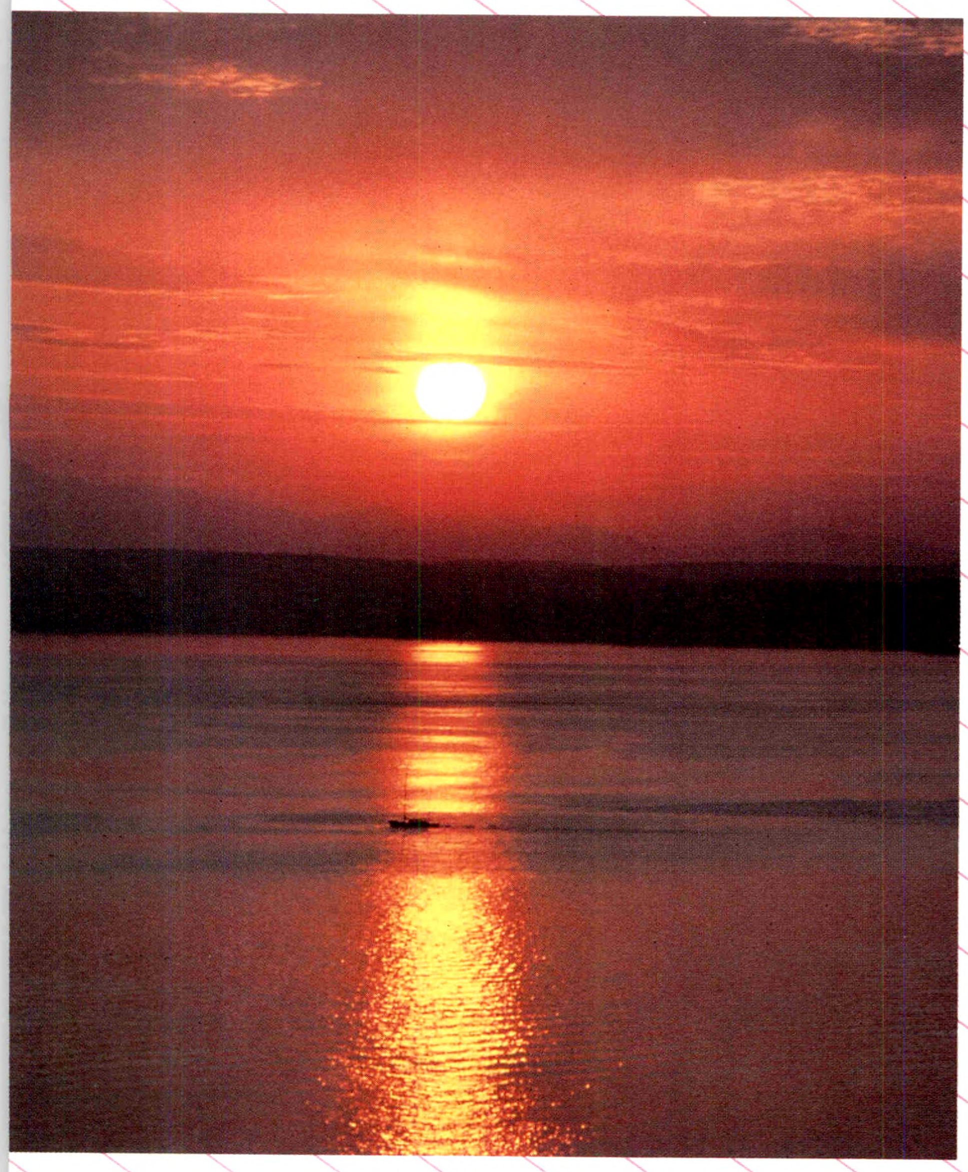

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Editorial

CARDIAC SURGERY IN THE KINGDOM OF SAUDI ARABIA

The fields of cardiology and cardiac surgery have witnessed an unprecedented development, achieving diagnostic and therapeutic levels difficult to predict a few years ago. The vast majority of cardiac patients can now be effectively treated. Congenital malformations are being detected noninvasively with two-dimensional echocardiography in infants soon after birth and sometimes even in utero. Most defects can be repaired in infancy or at least effectively palliated. Patients with valve disorders can experience dramatic improvement through insertion of the new valve prostheses, or through the use of the recently introduced valve repair techniques. Much is now known of the pathophysiology of ischemic heart disease. The use of thrombolysis for acute myocardial infarction and aggressively treating coronary stenosis with balloon dilatation or bypass surgery have changed the prognosis for patients with ischemia. Even the myocardiopathies, until recently outside the range of therapy, have benefited from the use of afterload reducing drugs and heart transplantation.

All these diagnostic and therapeutic modalities, however, require very costly human involvement and instrumental facilities that only a few countries can afford on a scale sufficient to meet the needs of the population. The continuous and apparently uncontrollable rise in health care costs are a source of concern for economists and political leaders around the world.

The status of the fields of cardiology and cardiac surgery in the Kingdom of Saudi Arabia is surprisingly positive and undoubtedly reflects the extraordinarily rapid development and modernization seen in virtually every technological aspect of the country. The first open-heart procedure was performed in Khamis Mushayt by the Loma Linda University team in 1976. Starting in 1978, open-heart surgery was performed on a regular basis at King Faisal Specialist Hospital, with the assistance of a team from Baylor University. The Armed Forces Hospital soon followed. More than 2,000 open-heart procedures are now performed every year in six centers, three in Riyadh and three in Jeddah, four of them in the public and two in the private sector. There are already five fully trained Saudi consultant cardiac surgeons, and a few more are about to finish their training, thus soon eliminating dependence on expatriate surgeons. The quality of surgery and cardiology performed in these centers meets the highest world standards. In fact, achievements in some particular areas, such as in valvular repair surgery performed at King Faisal Specialist Hospital and valvular dilatation as developed at the Riyadh Armed Forces Hospital, are regarded as pioneer and have attracted considerable international attention. Some of the symposia devoted to cardiology and cardiac surgery that have been held in the Kingdom have achieved the highest scientific level. However, the practice of cardiology and cardiac surgery in Saudi Arabia has left the exciting, initial phase of development and entered the demanding period of consolidation and universalization of those high levels achieved at its leading centers. This is an enviable position, given the extraordinary facilities offered by an enlightened administration, supportive authorities, and the possibility of learning from other experiences, both positive and negative, gained in other countries.

The number of centers necessary to meet the needs of a given population is difficult to establish according to any universal rule. Traditionally one center per million population has been considered sufficient to cover all the demand. However, this depends very much on the diagnostic ability and referral patterns in each area, and presupposes the incidence of the different pathological conditions is similar for every country. Furthermore, each open-heart unit must perform a minimum number of procedures each year to maintain the training of the team and assure continued results. Because of the high cost of supporting a cardiac facility, it must be fully employed. It is generally agreed that every unit must perform a minimum of 500 open-heart cases per year and should ideally do 1,000 per year. Generally, it is better to provide backup for existing units until they reach these targets before embarking into new ventures. Occasionally, geographic considerations make necessary the development of new units, although this does not apply in the Kingdom given the superb communication network and emergency transport system available.

The human factor in the provision of cardiology and cardiac surgery is even more important. With the current availability of first-rate consultants and future availability of a few young trainees in cardiac surgery, the needs of the country will soon be met. This is not the case for cardiologists, of which a much larger number is necessary given that at least every general hospital requires a cardiology unit. A warning seems appropriate at this point. Every cardiologist during his or her training is exposed to the catheterization laboratory and often to the therapeutic invasive techniques. Once back on a cardiology service, he or she wants to establish such a program, which should only be allowed with the backing of a cardiac surgery team. This attitude has given rise in some countries to a proliferation of centers that are sometimes not fully equipped and often without sufficient workload to justify their existence. A stronger emphasis on the noninvasive diagnostic techniques and better personal communication with the specialized centers should lead to improved quality of care and avoid professional frustration.

The training of specialized nurses and technicians probably constitutes the main problem facing cardiology and surgery in the Kingdom. There is a tremendous need for pediatric and intensive care nurses and technicians. The catheterization, electrocardiography, and echocardiography laboratories are still mostly staffed by expatriates who, though dedicated, are transient. The recent efforts of the Riyadh Armed Forces Hospital and King Faisal Specialist Hospital to start courses in cardiovascular technology are to be encouraged. This is another wide-open field for young Saudis who wish to develop their skills and apply their enthusiasm. The ongoing education of all cardiology-related health personnel is also important, and the very successful efforts of the still young Saudi Heart Association in this regard must be supported by all concerned. The achievements made in cardiology and cardiac surgery in Saudi Arabia serve as recognition of all those who made it possible. The future is bright, provided we all continue to work toward it.

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Original Articles

INTRACRANIAL MENINGIOMAS: ANALYSIS OF 53 CONSECUTIVE CASES WITH SPECIAL REFERENCE TO THEIR OPERABILITY AND SURGICAL OUTCOME

Zain Alabedeen B. Jamjoom, MD; Tajuddin Malabarey, FRCR; Saleem Sadiq, MB, BS, MPhil;
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أجري تحليل مراجعة لثلاث وخمسين حالة ورم سحائي داخل القحف وذلك وفقا للعمر والجنس والتوزيع والموضع التشريحي وطريقة العرض والعلاج الجراحي والنتيجة النهائية. تراوحت أعمار المرضى من ٢٥ إلى ٨٠ عاما (المتوسط ٤٧,٧ عاما) كانت نسبة الذكور الاجمالية للاناث ١ : ١,٩. وكانت مواضع الورم على النحو التالي: ٢٦,٤٪ في الحرف الوتدي، ٢٠,٨٪ في باطن قبة الجمجمة، ١٧٪ في المنطقة السهمية أو جوار السهمية، ١٣,٢٪ في الحفرة الشمية، ١١,٣٪ فوق السرج، ٩,٤٪ تحت الخيمة و١,٩٪ في مواضع متعددة. كان تأخر التشخيص والاحالة من السمات المألوفة لهذه الحالات مما أدى إلى إصابة أعداد كبيرة من المرضى بعيب عصبي شديد أو عمى.

أجريت لاثنين وأربعين مريضا سبعة وأربعون عملية جراحية لاستئصال الورم، وخضع ثمانية وثلاثون منهم للعملية الجراحية لأول مرة وأما التسعة الباقون فأجريت لهم العملية الجراحية لاصابات معاودة. كانت نسبة استئصال الورم كاملا في ٦١٪ في الذين أجريت لهم العملية الجراحية لأول مرة و٣٣٪ للعمليات المتكررة، تحققت أعلى المعدلات في آفات باطن القبة (١٠٠٪) وأدنى المعدلات في الأورام السحائية القاعدية (٢٩٪). كانت النتيجة عقب العملية الجراحية الأولى ممتازة في نسبة ٣٧٪ وتتراوح ما بين الجيدة والمقبولة في نسبة ٣٩٪، وضعيفة في نسبة ٨٪ من الحالات. كان عدد إجمالي الوفيات عقب العملية الجراحية ٦ (١٦٪)، إلا أن نسبة الوفيات في خلال ثلاثين يوما من العملية الجراحية كانت ٥,٣٪. كانت نسبة معاودة الاصابة عقب الاستئصال الكامل ٥,٦٪ وعقب الاستئصال الجزئي ٣٠٪. تشير هذه النتائج إلى أهمية التشخيص المبكر وتقديم العلاج اللازم للورم السحائي داخل القحف.

Fifty-three cases of intracranial meningiomas were retrospectively analyzed with regard to the age and sex distribution, anatomic location, mode of presentation, surgical management, and outcome. Patient age ranged from 25 to 80 years (average, 47.7 years); overall male to female ratio was 1:1.9. Tumor locations were: 26.4% sphenoidal ridge, 20.8% convexity, 17% sagittal or parasagittal, 13.2% olfactory groove, 11.3% suprasellar, 9.4% infratentorial, and 1.9% multiple. Delayed diagnosis and referral were common and accounted for a higher number of patients with severe neurologic deficit and blindness. Forty-two patients underwent 47 surgical procedures for tumor removal; 38 were first operations and 9 were for recurrences. Tumor removal was total in 61% of the first and 33% of the repeat operations; the highest rates were achieved for lesions in the convexity (100%) and the lowest for basal (29%) meningiomas. Outcome following first surgery was excellent in 37%, good to satisfactory in 39%, and poor in 8% of the cases. There was a total of 6 (16%) postoperative deaths; however, the 30-day postoperative mortality was 5.3%. The recurrence rate was 5.6% after total and 30% after partial resection. Our results emphasize the importance of early diagnosis and treatment of intracranial meningiomas.

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Because they are usually benign extracerebral lesions, meningiomas belong to that group of intracranial neoplasms most amenable to treatment, with a good prospect for permanent cure. However, because they grow slowly, they quite often reach considerable size before diagnosis. This, together with their frequent location at the base of the brain where they tend to encircle vital structures, has rendered the surgical treatment of meningiomas a challenging undertaking for even the most skilled and experienced neurosurgeon.

Findings from the evaluation of different hospital series of intracranial tumors have recently suggested that meningiomas are probably more common in Saudi Arabia than in European and Asian countries.[1-3] However, data concerning the age and sex distributions, anatomic locations, mode of presentation, and standards of management of meningioma in Saudi Arabia have been deficient. This has prompted our study of intracranial meningiomas in this country. We conducted a retrospective analysis of the clinical and radiologic features of patients with intracranial meningiomas treated in the Neurosurgical Division of the King Khalid University Hospital. Special attention was given to the operability of these lesions and surgical outcome. We compared our results with relevant data from the literature concerning epidemiology, clinical presentation, operability, and surgical outcome.

Analysis of Cases

Between 1983 and 1988, a total of 53 patients with intracranial meningiomas were diagnosed and treated at the King Khalid University Hospital in Riyadh. These cases constitute 22.7% of all intracranial tumors treated during this period. All patients underwent at least one cranial computed tomographic (CT) scan, and cerebral angiography was performed in the majority. There were 18 males and 35 females ranging between 25 and 80 years of age (average age, 51.1 years for males and 46.0 years for females). Seventy percent of the patients were between 40 and 60 years of age (Figure 1).

Location of Tumors

The anatomic distribution within the intracranial cavity was as follows: nine sagittal or parasagittal, 11 convexity, seven olfactory groove, six suprasellar, 14 sphenoidal ridge, and five infratentorial (Table 1). One patient had multiple supratentorial and infratentorial meningiomas. There were no pure intraorbital meningiomas in our series, but two of the sphenoidal ridge meningiomas had some intraorbital extension. The mean age of manifestation and the sex ratio seem to vary for meningiomas of different locations. Olfactory groove meningiomas tend to present an average of ten years later than those in other intracranial sites. In addition, there is a higher preponderance of females with basal meningiomas than with lesions in the convexity.

Clinical Features

The most common manifestations were headache, visual disturbances, and convulsions, present singly or in combination in nearly all patients (Figure 2). Headache was nonspecific

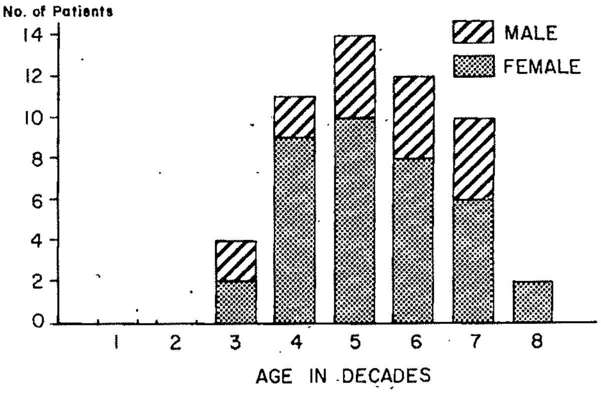

FIGURE 1. Age and sex distribution of 53 cases of intracranial meningiomas.

TABLE 1. *Anatomical distribution, sex ratio, and age of manifestation of intracranial meningiomas.*

Location	No. of patients	%	M:F	Mean age
Sagittal & parasagittal	9	17.0	2:1	45.7
Convexity	11	20.8	1:1.75	48.5
Olfactory groove	7	13.2	1:2.5	55.3
Suprasellar	6	11.3	1:2	40.8
Sphenoidal ridge	14	26.4	1:3.7	46.5
Infratentorial	5	9.4	1:4	50.6
Multiple	1	1.9	–	–
Total	53	100.0	1:1.9	47.7

and was encountered nearly equally in meningiomas of the different locations. In contrast, visual disturbances were almost invariably indicators of suprasellar, sphenoidal ridge, or huge olfactory groove tumors. Preoperative convulsions were documented in 40% of all patients, most commonly in those with convexity meningiomas and less frequently in association with large basal tumors. Duration of symptoms ranged from a few weeks to 30 years (average, 43.0 months). In more than 70% of the patients, symptoms had lasted more than one year. Generally, convulsions were the most long-standing complaint, exceeding 20 years in three cases. However, it was not unusual for visual disturbance to have been present for several years.

Reduction of visual acuity was the most common single neurologic finding (present in 39.6% of the patients) (Figure 3). In one third of the cases, the visual impairment was bilateral. Eight patients were blind, three bilaterally. Papilledema was rather uncommon, and therefore an unsuitable sign for excluding intracranial meningiomas. Thirteen patients were neurologically intact.

Based on their neurologic state and functional performance, the patients were classified into four clinical grades (Table 2). Patients in grade 1 were predominantly those with meningiomas of the vault.

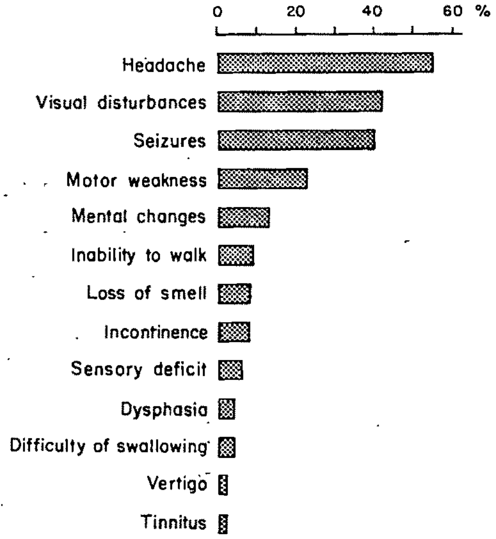

FIGURE 2. Incidence of symptoms at the time of admission in all meningiomas (N = 53).

Surgical Treatment

Forty-two patients underwent a total of 47 surgical procedures for removal of the tumor; 38 were first operations and the remaining nine were for recurrences. One patient had only a ventriculoperitoneal shunt installed for occlusive hydrocephalus caused by a posterior fossa meningioma. In four cases, the tumor was considered inoperable for various reasons: the first was an American woman who had had 13 previous operations for recurrent tumor with new growth invading the paranasal sinuses and scalp; the second was a 60-year-old totally disabled and demented woman with a huge olfactory groove meningioma engulfing the right carotid artery; the third patient

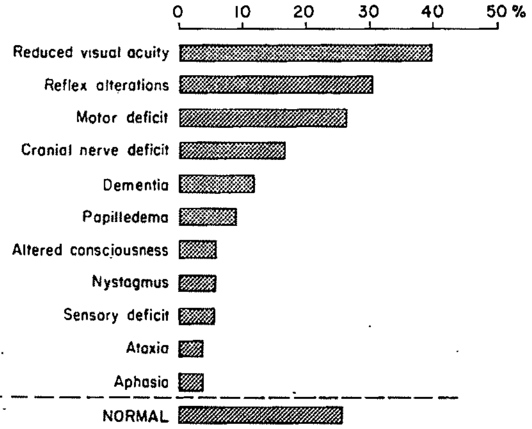

FIGURE 3. Incidence of neurologic findings at the time of admission in all meningiomas (N = 53).

TABLE 2. *Preoperative clinical grade in relationship to intracranial location of the meningioma.*

	Clinical grade*				
Location	I	II	III	IV	All
Sagittal & parasagittal	2	4	1	2	9
Convexity	6	2	1	2	11
Olfactory groove	2	1	1	3	7
Suprasellar	0	2	4	0	6
Sphenoidal ridge	2	6	5	1	14
Infratentorial	1	0	1	3	5
Multiple	0	0	0	1	1
Total	13	15	13	12	53

*I = no neurologic deficit; II = neurologic deficit but able to work; III = neurologic deficit but able to care for self; IV = requires assistance and care.[30]

was an elderly woman with hepatic failure; and the fourth was a young woman with a meningioma en plaque that invaded the left cavernous sinus and constricted the left carotid artery. The remaining six patients refused surgery.

Of the 38 meningiomas operated on for the first time, 23 (61%) were excised totally. In the remaining 15 (39%), residual tumor of varying degree was left in situ. The highest rates of complete removal were achieved for meningiomas located in the convexity (100%) followed by those in the falx and olfactory groove (67%). For the basal meningiomas, total removal could be accomplished in only five of 17 cases (29%) (Table 3) (Figure 4).

Seven patients were operated on for recurrence or progression of incompletely removed meningioma. Of these, three patients had their first operation at KKUH; the remaining four had undergone operation once or several times previously in other hospitals. One patient had a two-stage procedure, and another underwent a third operation for further progression of the tumor. Of the nine repeat craniotomies, total removal of the tumor was possible in only three (33%) (Figure 5).

The histopathologic diagnosis of the 42 surgically treated cases was based on the classification adopted by Russel and Rubinstein.[4] The transitional forms were most common, while the malignant variant was absent among our patients (Table 4).

Outcome

The postoperative versus preoperative clinical grades of the 38 patients who underwent first tumor resection are shown in Figure 6. The

TABLE 3. *Degree of first tumor resection in 38 meningiomas of various locations.*

	Resection		
Location	Total	Partial	Total
Sagittal & parasagittal	5	1	6
Convexity	9	–	9
Olfactory groove	4	1	5
Suprasellar	1	4	5
Sphenoidal ridge	3	5	8
Infratentorial	1	3	4
Multiple	–	1	1
Total	23(61%)	15(39%)	38(100%)

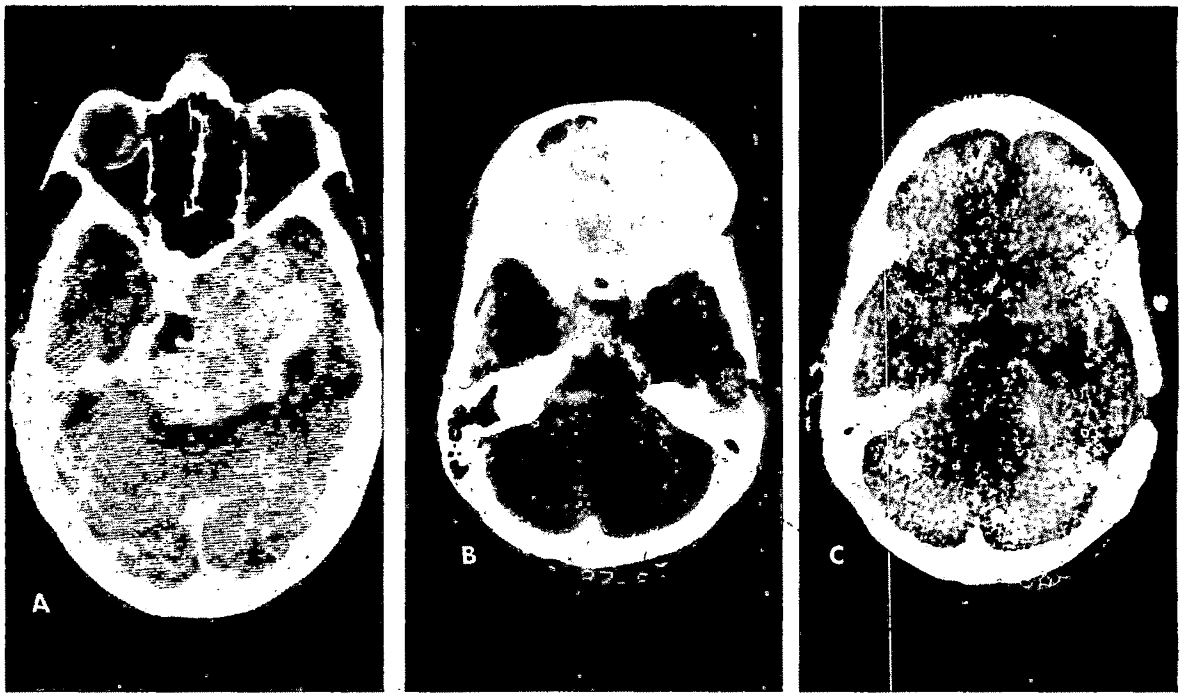

FIGURE 4. (A) Preoperative CT scan of an extensive medial sphenoidal ridge meningioma growing into the tentorial hiatus. The patient was a 45-year-old woman who presented with impaired vision in the right eye, right-sided facial weakness, and difficulty swallowing for 3 years. (B,C) Postoperative CT scans demonstrating complete excision of the tumor.

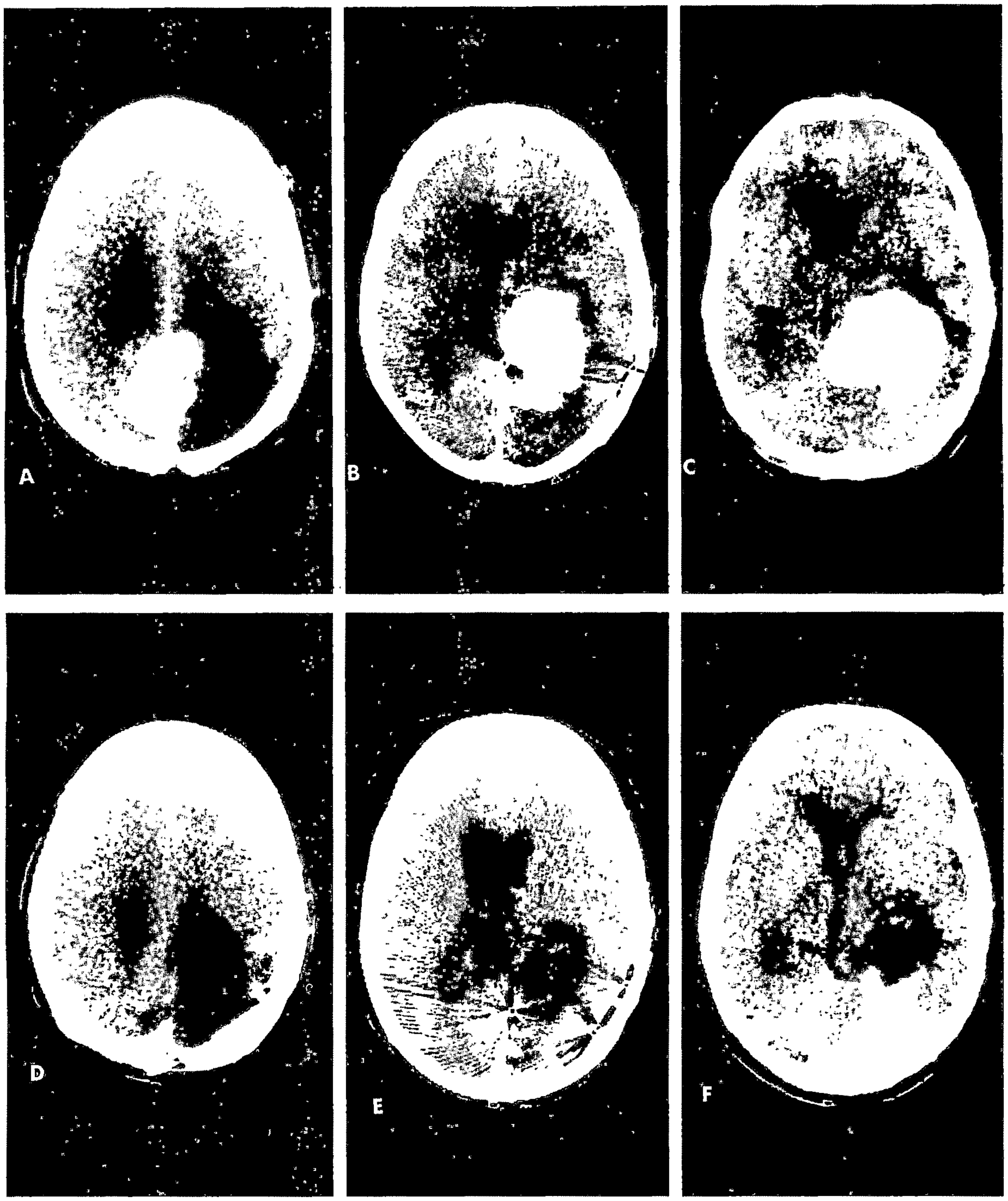

FIGURE 5. (A-C) Preoperative CT scan of a third recurrence of a meningioma of the posterior third of the falx in a 40-year-old woman. The main bulk of the tumor is subfalxial with its attachment at the falx-tentorium junction. (D-F) Postoperative CT scan confirming total removal of the tumor.

neurologic state was unchanged in 16 (42%), improved in 11 (29%), and deteriorated in five (13%) patients. The remaining 16% represent all the postoperative fatalities (defined as deaths in hospital from any cause following operation).

For the evaluation of surgical results, two

TABLE 4. *Histopathologic subtypes of the 42 operated meningiomas.*

Histologic subtype	No. of patients	Percentage
Syncytial	10	23.8
Transitional	17	40.5
Fibroblastic	13	30.9
Angioplastic	2	4.8
Malignant	–	–
Total	42	100

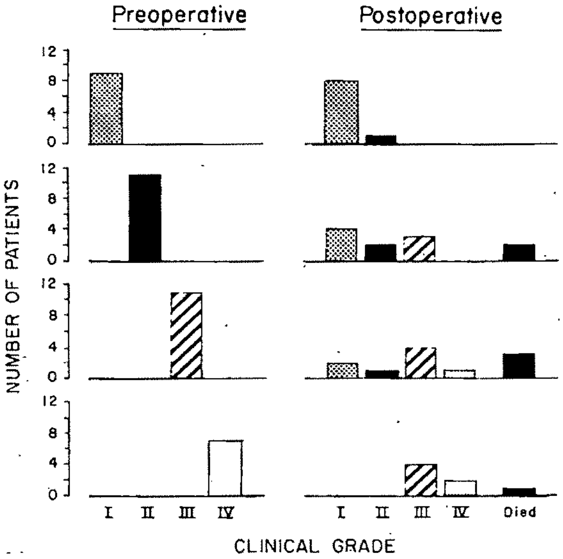

FIGURE 6. Comparison of postoperative and preoperative clinical grade in the 38 patients undergoing first tumor resection.

TABLE 5. *Surgical results in relationship to intracranial site of the meningioma.*

	Surgical result					
Location	Excel-lent	Good	Satis-factory	Poor	Died	All
Sagittal & parasagittal	4	0	1	1	0	6
Convexity	7	0	1	0	1	9
Olfactory groove	2	0	2	1	0	5
Suprasellar	0	2	2	0	1	5
Sphenoidal ridge	0	1	3	1	3	8
Infratentorial	1	0	2	0	1	4
Multiple	0	0	1	0	0	1
Total	14	3	12	3	6	38

criteria were considered: (1) the extent of tumor removal and (2) the postoperative clinical grade of the patient. The outcome was considered excellent if the patient was neurologically normal following complete removal of the tumor. Improved postoperative neurological state and unchanged preoperative neurological deficit following incomplete tumor resection constitute good and satisfactory outcome, respectively. Poor outcome was assumed whenever incomplete tumor excision resulted in deterioration of the patient's neurostatus. Of the 38 cases operated on for the first time, surgical outcome was excellent in 14 (37%), good to satisfactory in 15 (39%), and poor in three (8%) patients (Table 5). Meningiomas of the convexity have a more favorable prognosis than those of the base, meningiomas of the falx and olfactory groove having an intermediate prognosis. Two of the six postoperative deaths were due to acute cardiopulmonary complications during the early postoperative period; three patients succumbed to opportunistic infections after a period of postoperative coma lasting from 2 to 13 months, and probable drug-induced severe thrombocytopenia developed in one patient, accompanied by fatal hemorrhagic diasthesis, five weeks after operation. The 30-day postoperative hospital mortality rate for these 38 patients was 5.3%.

Recurrence

Twenty-eight of the 32 patients who survived the first operation were followed up from two to 57 (average, 23) months. True recurrence developed in one patient two years following total removal of a parietal meningioma. Of the survivors who had total tumor resection (18 patients), the incidence of true recurrence was 5.6%. In contrast, three of the ten survivors who underwent incomplete tumor removal showed progression of the residual tumor within an average follow-up time of two years.

The surgical outcome in the seven patients who were operated on for tumor recurrence or progression was excellent in one (14%) and good to satisfactory in three (43%). The remaining three patients died from meningitis, diabetic coma and cerebral infarction, and pulmonary embolism, respectively.

Discussion

The incidence of intracranial meningiomas in our hospital series in Saudi Arabia ranges between 22.8 and 27% of all intracranial neoplasms.[1-3] These figures are higher than those reported from European and Asian countries,[5-10] but comparable to the percentages derived from Africa.[11-13] Both age and sex distributions of our patients are within the reported limits.[5,14,19] The earlier occurrence in females than males in this series agrees with observations of Cushing[5] published fifty years ago. It has been suggested that the higher estrogen and progesterone levels in the female might influence the growth of meningiomas.[20,21] The intracranial distribution of the meningiomas in our series agrees with that noted in other large series.[5,14-19] Meningiomas of the base were more predominant in females than were those in the vault.

The 40% incidence of preoperative convulsions in our patients is very similar to recent figures in the literature.[18,22] In contrast, visual impairment was unusually high among our patients, but this cannot be explained by the slightly higher proportion of basal meningiomas in our series. Delayed diagnosis and referral are more probable reasons. The average time interval between first symptoms and diagnosis of 43.0 months is almost twice that reported in other series.[18,19] The patients were not always responsible for the delayed diagnosis. There were several instances in which patients had gone from one physician to another before proper investigations were carried out and diagnosis made.

Surgical excision is the method of choice in the management of meningiomas. However, tumor removal should be only as radical as is safe for the patient. As borne out by other series, the extent of tumor resection depends mainly on the location of the tumor.[19,23] While radical excision is usually possible for convexity meningiomas, it may prove difficult or even impossible in falx meningiomas without resection of the superior sagittal sinus.[24,26] This maneuver may be permissible in the anterior third of the sinus or when the sinus has been totally occluded by tumor invasion, but the effects of ligating the patent posterior two thirds of the sinus are frequently deleterious. The technical problems associated with operations for removal of medially situated basal meningiomas are even more pronounced. Complete resection of these tumors is frequently limited by their relationship to major cerebral blood vessels and/or vital neural structures, and is achieved in 20 to 40% of the cases, depending on the exact location of the tumor.[19,27-30] In this series, total removal could be achieved in only five of the 17 (29%) cases of basal meningiomas of various locations.

Both immediate and late surgical outcome in patients with intracranial meningiomas are determined mainly by the location of the tumor and the degree of tumor resection. Sixty-five percent of the patients with parasagittal, convexity, and olfactory meningiomas in the present series were either normal or had only mild neurologic deficits postoperatively. In contrast, only 29% of the patients with sphenoidal ridge, suprasellar, or posterior fossa tumors achieved such good results. Similarly, while 65% of the patients who had complete tumor removal returned to normal activities, only 20% of those with partial excision were able to do so. This is consistent with the findings of other authors.[18,23] The influence of the patient's preoperative neurologic state on outcome cannot be ignored. Generally, the surgical prognosis is better in patients without than in those with a preoperative neurological deficit. Since the preoperative neurologic state depends, among others, on the size of the meningioma, the importance of early recognition cannot be overemphasized.[27] Chan et al[18] found that patients with meningiomas measuring 4.5 cm in diameter or less had a significantly better prognosis than those with tumors measuring 7 cm or more in diameter.

The operation-related mortality varies considerably from one series to another, ranging from 4.3 to 17.8%[5,15-19,22,31] and even higher.[14] In our series, the overall postoperative hospital mortality after first tumor resection was 16% and this is comparatively high. This is probably the result of long postoperative hospitalization of patients in poor but otherwise stable neurologic condition. It has been frequently difficult to transfer such patients back to their regional hospitals, and so they tend to remain for lengthy neurosurgical care with ultimate death in hospital. The one-month postoperative hospital mortality may provide a better basis for comparison, which in our series was 5.3%. This is very similar to the rates reported by other authors.[15,18]

The overall recurrence rate of intracranial meningiomas ranges between 10.5 and 22% in most series,[16-19,32] and was 14.3% in the present study. Simpson[23] and subsequently several other authors[17-19,26] have clearly demonstrated that the extent of the first tumor resection is the most important single factor that determines the rate of recurrence. Failure to excise the dural attachment following total tumor removal was found to increase the chance of tumor recurrence from approximately 10 to 20% if the site of attachment was cauterized, and even 29% if it was not.[18,23] Tumor progression after incomplete removal occurred in as many as 37 to 52% of the cases.[17-19,23] In the present series, the short follow-up periods (average, 23 months) account for the comparatively low rates of tumor recurrence and progression (5.6% and 30%, respectively). Recent studies using life-table analysis have shown that the probability of recurrence or progression increases with the duration of the postoperative follow-up period.[17,19] In our experience and that of others,[26] morbidity and mortality are higher for the second than the first tumor resection. Nevertheless, operations for meningioma recurrence are frequently rewarding.[23,26]

The ability of meningiomas to recur after radical excision suggests that factors other than the degree of tumor removal could also play a role. Borovich and Doron[33] were able to demonstrate several separate aggregates of meningotheliomatous cells within or on the inner surface of the dura mater surrounding solitary globular meningiomas, and suggested that regional multicentricity may be responsible for tumor recurrence after total resection. Some authors reported a higher recurrence potential for meningiomas of certain locations. Giombini et al[26] found a recurrence rate of 18.1% following radical excision (i.e., including dural attachment) of 187 parasagittal and falx meningiomas, whereas only 4.3% of their 93 olfactory and suprasellar meningiomas recurred despite less radical removal (i.e., without dural attachment). Four of our seven patients operated on for tumor recurrence had sagittal or parasagittal meningiomas. Except for the malignant forms, the histologic features of meningioma seem to have little influence on its rate of recurrence,[23] but some authors also ascribe to the angioplastic meningiomas a higher potential of recurrence.[17,32] The frequency of the different histologic subtypes in our patients is, except for the absence of the malignant form, quite similar to that in other series.[17,18] None of the seven cases of recurrent meningioma in our series was angioblastic or malignant, and the other histologic subtypes were present equally.

There are no well-defined criteria for determining an inoperable meningioma. Only a few authors refer to unoperated cases in their series. Chan et al[18] reported that 25 of 299 (8.4%) patients with intracranial meningiomas were not operated on for various reasons, including high surgical risks. In a recent series, Pertuiset et al[22] operated on 80 cases of intracranial meningiomas, but during the same time, they refused surgery in 15 (15.8%) cases because of what they called "surgical incurability" of the tumors. Reasons given were the mediobasal location of the tumor with encroachment on major vessels and other neural structures in 12 cases, poor preoperative level of consciousness in one, and irreversible loss of vision in two. In the present series, surgery was deferred in cases of extensive (and repeated) tumor recurrence, long-standing severe neurologic disability, irremediable organ failure, and wide en plaque growth of the tumor with infiltration and/or constriction of major cerebral vessels.

The role of radiotherapy in the management of meningiomas is still controversial. Simpson[23] found little evidence of permanent benefit in 28 cases of meningiomas treated with irradiation. More favorable results were achieved by Wara et al[34] who reported a regrowth rate of 29% in 34 cases of partially excised meningiomas followed by radiotherapy, compared with 74% in 58 other patients treated by surgery alone. In one study, radiotherapy was found to be more effective when given directly after partial tumor resection rather than after recurrence.[35] Yamashita et al[16] also concluded that irradiation is of little value in recurrent meningiomas. In the present series, postoperative radiotherapy was not advocated in any of the patients. We agree with Simpson[23] who stated that "when a meningioma has actually recurred, experience here justifies a second operation on the most radical scale, even at greater hazard than would ordinarily be accepted."

Conclusion

Available data suggest that meningiomas are probably more common in Saudi Arabia than in Europe and Asian countries. However, there were no significant differences regarding age and sex distributions, intracranial locations, and histologic subtypes. Delayed diagnosis and referral for very long periods are still the rule rather than the exception, and were responsible for higher numbers of patients presenting with severe neurologic deficits and blindness. Surgical excision is the method of choice in the management of meningiomas, but certain anatomic locations rule out safe excision of the whole tumor. With the exception of the malignant form, postoperative outcome for meningiomas is mainly determined by the site of the lesion and the extent of removal. At present, the role of radiotherapy in the management of meningiomas is still limited. It is hoped that with the widespread use of CT scanning throughout the Kingdom, these lesions will be discovered at an earlier stage when they are small and better accessible to surgery. Despite the technical advances in neurosurgery during the past two decades, mediobasal meningiomas still represent a therapeutic challenge and a field for new developments.

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HEMOSTASIS IN PREGNANT SAUDI WOMEN

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أجريت دراسة عن متغيرات الإرقاء المختلفة لدى عينة نموذجية من النساء خلال الأثاليث الثلاثة من الحمل الطبيعي. لوحظ خلال الأثلوث الثالث ارتفاع هام في فبرينوجين البلازما ٥٥٪، وفي نشاطات العامل الثامن ٦٤٪، وفي العامل الثامن: تميم الريستوسيتين ٤٤٪، والمستضد المتصل بالعامل الثامن ٤٩٪، والعامل العاشر ٩٪، ومولد البلزمين ١٩٪، وانخفاض في مضاد الترمبين الثالث ١٠٪، وألفا ٢ـ مضاد البلزمين ٧٪، وفي عدد الصفيحات ٢٠٪، كل ذلك بالمقارنة مع النتائج التي حصلنا عليها لدى مجموعة الضبط من صحيحات الجسم غير الحوامل. وقد نشأت هذه التقلبات تدريجيا خلال الأثلوثين الأول والثاني. أما زمن البروترمبين وزمن الترمبوبلاستين الجزئي وزمن الترمبين وزمن الريبتيلاز فكانت متماثلة لدى الحوامل وغير الحوامل. وكانت تكدس الصفيحات استجابة لثاني فسفات الأدينوزين والكلاجين والأدرينالين وحمض الأراكيدونيك لدى الحوامل أقل بدرجة هامة عن ما هو عليه لدى غير الحوامل. إن انخفاض تكدس الصفيحات لدى الحوامل السعوديات قد يكون له تأثير معدل للزيادة في خطر التخثر البلزمي وبالتالي يقلل من خطر مرض الانصمام الخثاري أثناء الحمل.

A cross-sectional study of various hemostatic variables was undertaken in women during the three trimesters of normal pregnancy. In the third trimester of pregnancy, there was significant elevation of plasma fibrinogen, 55%; factor VIII activities, 64%; factor VIII:ristocetin cofactor, 44%; factor VIII-related antigen, 49%; factor X, 9%; and plasminogen, 19%, and a reduction of antithrombin III, 10%; alpha$_2$-antiplasmin, 7%; and platelet count, 20%, compared with those values obtained in healthy nonpregnant controls. These fluctuations developed gradually during the first and second trimesters. Prothrombin time, partial thromboplastin time, thrombin time, and reptilase time were similar in pregnant women and nonpregnant controls. Platelet aggregation in response to adenosine diphosphate, collagen, adrenaline, and arachidonic acid was significantly reduced in pregnant women compared to controls. The reduced platelet aggregability in Saudi pregnant women may counterbalance the increased plasmatic coagulation potential, thereby minimizing the risk of thromboembolic disease during pregnancy.

It is now well established that pregnancy produces an increase in the concentration of plasma fibrinogen and coagulation factors VIII, IX, and XII; a reduction in the level of antithrombin III; and depression of fibrinolytic activity.[1] These physiological adaptations of the hemostatic mechanism are unique to human pregnancy and represent a hypercoagulable state[2] that assures rapid and effective hemostasis during parturition. However, such a normal physiological situation is potentially dangerous, as it increases the risk of thromboembolic disease in pregnancy and exposes pregnant women to the risk of severe hemorrhage in the event of acute coagulation failure.[1]

The management of various hemostatic disorders during pregnancy depends on laboratory measurements of various components of the hemostatic system, so that suitable therapeutic measures may be administered and monitored.

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This study was therefore undertaken to establish baseline normal levels of hemostatic variables in Saudi women.

Subjects and Methods

The subjects represented a cross section of Saudi nationals who were selected randomly from the antenatal clinic at the Riyadh Maternity Hospital. A careful medical and obstetrical history was taken, and only those with a normal complication-free pregnancy who were not under any form of drug therapy were selected. Patient data are shown in Table 1.

Blood for coagulation assays was drawn directly into citrate-containing syringes (Monovette System; Sarsdt, West Germany) to give a blood-citrate ratio of 9 to 1. Blood for platelet count was collected in EDTA-containing tubes, and for serum fibrin degradation products (FDP) assay in plain plastic tubes.

Processing of blood for coagulation assays and platelet aggregation has been detailed elsewhere.[3-5] Samples for coagulation assays were transported in ice to the laboratory, where plasma was separated at 4°C and stored at –40°C for analysis at a later date. Platelet-rich plasma (PRP) used for platelet aggregation studies was prepared by centrifuging citrate blood samples at 150 *g* for seven minutes at room temperature (23°C). Using a plastic pipette, PRP was separated and kept in a stoppered plastic container. The remaining blood specimen was centrifuged at 1500 *g* for 15 minutes, and the platelet-poor plasma (PPP) was removed and used as the standard for the turbometric aggregation studies, carried out according to the method of Gader et al.[5]

Coagulation Tests

The following tests were performed as described previously,[3,4] unless otherwise indicated: prothrombin time (PT); partial thromboplastin time (PTT; Ortho-diagnostic reagents); thrombin time (Parke Davis Topical Thrombin); reptilase time (Pentapharm, Switzerland); plasma fibrinogen, using the turbometric method of Ellis and Stransky;[6] antithrombin III chromogenic assay,[7] using substrate S2238 (Coatest Kits; Kabi, Sweden); factor VIII:ristocetin cofactor, according to the method of Macfarlane et al;[8] serum fibrin degradation products (FDPs) by the hemagglutination inhibition immunoassay using FDP kits (Wellcome Reagents Limited, England); von Willebrand factor antigen (vWFAg), using a modification of Laurell's technique;[9] and platelet counts by a thrombocounter (Coulter Electronics). The following parameters were assayed by chromogenic substrates according to instructions of the manufacturers: plasminogen and alpha$_2$-antiplasmin (Berichrome kits; Behring, West Germany); factor VIII coagulant (factor VIII:C) and factor X (Coatest Kits; Kabi, Sweden). Normal pooled plasma used as control for these coagulation assays was obtained from 20 healthy nonpregnant volunteers and was taken to represent 100% activity of the various assays. These volunteers were blood donors, members of the teaching and technical staff, and students. There were 10 male and 10 female subjects aged 21 to 45 years (mean + SD = 29.5 + 6.9).

Platelet Aggregation

Platelet aggregation was performed in PRP in response to adenosine diphosphate (ADP) (20, 2.0, 1.0, and 0.5 μM/L), collagen (0.19 g/L), arachidonic acid (1.64 mmol/L), adrenaline (100 mmol/L), and ristocetin (150, 120, and 100 g/L), as detailed previously.[5] All concentrations of the aggregating agents were final concentrations obtained by adding 20 μl of agonist to 180 μl of

TABLE 1. *Age, weight, and height data in women with normal pregnancy.**

Trimester	Age (yr)	Weight (kg)	Height (cm)
First (N = 81)	28.0 + 7.3 (16–48)	64.9 + 15.4 (38.2–109)	156.4 + 6.4 (145–175)
Second (N = 169)	26.3 + 6.2 (15–45)	66.4 + 17.3 (36.5–121.3)	155.8 + 9.3 (125–180)
Third (N = 410)	27.0 + 5.9 (14–48)	72.2 + 15.3 (32.5–121.9)	156.3 + 6.7 (115–179)

*Values are expressed as the mean + standard deviation. Range is given in parentheses.

PRP in an aggregometer (Aggregation Profiler PAP4; Bio/Data Corp, U.S.A.).

The results obtained in the pregnant women were compared to reference values for healthy Saudi women, aged 12 to 50 years (to be published).

Students' t test was used to establish significance, defined as $P < 0.05$.

Results

Coagulation Test

There were no significant differences in the mean levels of PT, PTT, thrombin time, or reptilase time among women in the three trimesters or compared with nonpregnant controls. However, in comparing women in the third trimester with nonpregnant controls, there was a significant increase in plasma fibrinogen (55%); factor VIII activities: factor VIII:C (64%), factor VIII:ristocetin cofactor (44%), and vWFAg (49%); factor X (9%); and plasminogen (19%); and there was a reduction in antithrombin III (10%), alpha$_2$-antiplasmin (7%), platelet count (20%), and packed cell volume (90%). Similar smaller changes were observed in women in their first and second trimesters.

Comparison of hemostatic variables among trimesters revealed significantly higher levels of fibrinogen ($P < 0.05$), vWFAg ($P < 0.001$), and factor VIII:C ($P < 0.005$) in the third compared to second trimester. Smaller fluctuations were noted between the second and first trimesters, but statistical significance was observed only for alpha$_2$-antiplasmin ($P < 0.05$). The packed cell volume was comparable for all three trimesters. Table 2 shows a summary of the various hemostatic variables and the values obtained.

Platelet Aggregation

There was a statistically significant diminution of the platelet aggregation responses to ADP, collagen, adrenaline, and arachidonic acid in women in the three trimesters of pregnancy compared to nonpregnant controls. There was also evidence of increased responses to ADP (2.0 and 1.0 μM; $P < 0.01$) and adrenaline ($P < 0.05$) in the third compared to second trimester. There was also increased response to ADP (1.0 μM; $P < 0.05$), ristocetin, and collagen ($P < 0.01$) in the first com-

TABLE 2. *Blood coagulation parameters in normal pregnant women and nonpregnant controls.*

	Mean ± SD			
Variables	1st trimester	2nd trimester	3rd trimester	Control (range)
PT (sec)	11.8 ± 0.8(43)	11.8 ± 1.0 (106)	11.8 ± 1.2 (409)	11.8 ± 0.9 (375)
PTT (sec)	27.0 ± 4.4 (43)	28.3 ± 4.8 (102)	26.8 ± 5.4 (403)	26.8 ± 2.8 (375)
TT (sec)	13.5 ± 4.2 (39)	13.2 ± 3.5 (102)	16.4 ± 3.4 (394)	16.7 ± 3.1 (365)
RT (sec)	12.3 ± 1.7 (35)	12.1 ± 1.4 (76)	12.1 ± 1.7 (331)	11.9 ± 1.1 (294)
FIB (g/L)	421.4 ± 146.3 (32)†	442.8 ± 123.1 (77)§	479.5 ± 131.3 (228)§	309.1 ± 74.5 (281)
AT III (%)	89.6 ± 12.7 (33)§	90.0 ± 13.6 (73)§	93.4 ± 29.5 (230)§	103.5 ± 12.1 (234)
FDPs (%)	3.8 ± 3.1 (13)	8.0 ± 7.9 (20)	10.5 ± 9.8 (26)	4.2 ± 3.7 (30)
Plasminogen (%)	123.7 ± 22.2 (25)*	130.2 ± 24.4 (48)§	134.2 ± 20.2 (147)§	112.5 ± 15.0 (176)
a2ANTPLS (%)	104.0 ± 12.8 (25)	96.2 ± 12.9 (47)	92.0 ± 12.6 (147)§	98.6 ± 13.3 (176)
RICOF (%)	148.0 ± 109.9 (30)*	147.5 ± 84.6 (57)*	161.4 ± 91.6 (217)§	111.8 ± 35.0 (103)
vWF Ag (%)	212.2 ± 70.3 (10)†	237.3 ± 66.1 (22)§	288.9 ± 104.2 (83)§	111.1 ± 46.3 (151)
FVIII:C (%)	135.9 ± 65.1 (28)*	138.7 ± 57.7 (43)§	180.9 ± 63.4 (183)§	113.3 ± 60.2 (151)
Factor X (%)	105.1 ± 24.5 (19)	114.8 ± 22.6 (18)	122.6 ± 16.8 (46)	112 ± 21.3 (51)
PLTCNT ($\times 10^3$/mm^3)	252.7 ± 61.8 (28)	237.8 ± 66.4 (70)	223.4 ± 74.8 (270)§	277.8 ± 66.5 (274)
PCV (%)	36.7 ± 2.9 (20)	36.4 ± 7.5 (61)	36.4 ± 4.0 (244)	40.2 ± 3.2 (214)

*$P < 0.05$; †$P < 0.005$; § $P < 0.001$, comparing each trimester of pregnancy with controls.

PT = prothrombin time; PTT = partial thromboplastin time; TT = thrombin time; RT = reptilase time; FIB = plasma fibrinogen; AT III = antithrombin III; FDPs = fibrin degradation products; a2ANTPLS = alpha2-antiplasmin; RICOF = ristocetin cofactor; vWFAg = von Willebrand factor antigen; FVIII:C = factor VIII coagulation; PLTCNT = platelet count; PCV = packed cell volume.

pared to second trimester. Table 3 summarizes the platelet aggregation findings for the study groups and nonpregnant controls.

Discussion

This study revealed the standard values of various hemostatic variables for normal pregnancy in Saudi women. The most consistent observation has been the progressive increase in fibrinogen content from the first trimester onward. This observation has been confirmed by other reports.[10-17] Turnover studies have shown that this increase in fibrinogen level is the result of increased synthesis by the liver.[16]

We also noted a progressive rise in factor VIII activities (factor VIII:C, ristocetin cofactor, and vWFAg), especially in the second and third trimesters, and this agrees with findings from earlier reports.[11,15,17-21] In the present study, the vWFAg/VIII:C ratios in the first, second, and third trimesters are 1.23, 1.7, and 1.6, respectively. Such elevated ratios are common in normal pregnancy[14,22,23] and are indicative of thrombin-induced loss of factor VIII:C activity as a consequence of activation of the coagulation system and thrombin generation.[14]

Weenink et al,[24] using the chromogenic substrate (S 2238) assay we used in this study, found no significant variation in the antithrombin III concentration throughout pregnancy and puerperium compared to nonpregnant levels. A similar conclusion was reported more recently by Stirling et al.[14] Our finding of a slight but statistically significant decrease in antithrombin III levels in the second and third trimesters of pregnancy confirms other reports[22,25] and could be other indirect evidence of thrombin generation.

Reports on platelet count in pregnancy have provided discordant results. In most studies, no significant changes were observed,[11,15,21,26,27] while in others, like our own, a slight reduction was found.[15,28,29] In contrast to these findings, Mor et al[30] found a marked and progressive increase in the platelet count during pregnancy and a sharp drop at the time of placental delivery. As with antithrombin III, the fluctuations in platelet counts, though statistically significant, were within the normal range for nonpregnant controls.

TABLE 3. *Platelet aggregation in normal pregnant women and nonpregnant controls.*

	Mean ± SD			
Variables	1st trimester	2nd trimester	3rd trimester	Control (range)
ADP2.0μM/L(S)	28.2 ± 8.4 (19)*	24.4 ± 9.0 (27)*	30.4 ± 10.0 (163)†	33.3 ± 10.6 (193)
ADP2.0μM/L(MA%)	41.4 ± 18.1 (19)*	46.0 ± 19.7 (27)*	56.7 ± 18.6 (163)*	50.7 ± 22.3 (193)
ADP1.0μM/L(S)	26.9 ± 6.3 (11)	18.1 ± 9.1 (15)†	26.4 ± 9.9 (116)	27.3 ± 8.8 (93)
ADP1.0μM/L(MA%)	25.9 ± 7.7 (11)*	26.5 ± 12.6 (15)*	39.3 ± 19.9 (116)	30.3 ± 21.3 (93)
ADP20.0μM/L(S)	34.8 ± 11.8 (5)	31.1 ± 6.7 (10)*	27.4 ± 11.4 (30)†	35.9 ± 9.6 (53)
ADP20.0μM/L(MA%)	48.4 ± 77.0 (5)	61.2 ± 9.5 (10)	56.6 ± 19.8 (30)	56.5 ± 16.3 (53)
ADR(S)	12.0 ± 6.8 (14)	13.0 ± 6.5 (25)*	17.2 ± 7.2 (131)*	14.0 ± 9.0 (184)
ADR(MA%)	39.4 ± 25.2 (14)*	51.9 ± 24.8 (25)	58.0 ± 19.0 (131)	53.5 ± 28.6 (184)
ARCH500μg/mL(S)	32.9 ± 14.9 (17)	28.5 ± 15.3 (22)*	33.6 ± 14.5 (138)	35.0 ± 12.9 (141)
ARCH500μg/mL/(MA%)	58.9 ± 23.8 (17)	52.7 ± 25.6 (22)*	59.0 ± 22.4 (138)†	68.5 ± 16.4 (141)
COL190μg/mL(S)	37.4 ± 13.6 (14)	32.5 ± 13.0 (22)*	31.7 ± 12.0 (145)†	39.3 ± 9.2 (187)
COL19μg/mL(MA%)	69.6 ± 15.0 (14)	57.3 ± 16.7 (22)†	60.6 ± 16.2 (145)	62.2 ± 13.1 (187)
RIST1.5mg/mL(S)	38.4 ± 14.3 (15)	33.6 ± 11.6 (22)*	37.3 ± 13.7 (145)*	42.1 ± 16.6 (169)
RIST1.5mg/mL(MA%)	73.9 ± 23.6 (15)	74.3 ± 14.3 (22)*	73.5 ± 18.0 (145)§	80.6 ± 15.5 (169)
RIST1.2mg/mL(S)	18.5 ± 8.6 (15)†	21.4 ± 12.0 (16)*	20.1 ± 13.7 (109)†	29.4 ± 13.9 (99)
RIST1.2mg/mL(MA%)	30.0 ± 19.6 (15)§	50.3 ± 31.4 (16)*	43.7 ± 28.3 (109)§	71.3 ± 20.4 (99)
RIST1.0mg/mL(S)	9.1 ± 5.5 (10)*	11.4 ± 6.6 (8)*	13.9 ± 9.7 (71)	19.4 ± 14.3 (46)
RIST1.0mg/mL(MA%)	10.2 ± 3.2 (9)§	23.0 ± 14.0 (8)†	28.6 ± 22.3 (71)†	51.6 ± 30.8 (46)

*$P < 0.05$; †$P < 0.005$; §$P < 0.001$, comparing each trimester of pregnancy with controls.
ADP = adenosine diphosphate; ADR = adrenaline; ARCH = arachidonic acid; COL = collagen; RIST = ristocetin.

The steady decline in fibrinolytic activity during pregnancy is believed to be due to both a placenta-derived inhibitor[1,11,31-33] and progressive decrease of plasminogen activator release by endothelial cells.[1,33,34] This fibrinolytic shut-down occurs despite the increased levels of plasminogen, as found in our and other studies.[11,31-33] Conversely, the plasma levels of the protease inhibitor alpha$_2$-antiplasmin during normal pregnancy was found to be both unchanged[35] and increased,[36,37] while in the present study we noted a slight decrease in the third trimester. These widely varying findings could be due to differences in assay techniques.

An aspect of in vitro fibrinolysis that has received much attention is the serum FDPs. The reported levels during normal pregnancy have also been inconsistent. While some investigations revealed a small rise in the third trimester,[35,38] others, including our study, have not been able to detect a significant change.[39,40] These disagreements in the fibrinolytic parameters during pregnancy emphasize further the need for improved assay techniques so that these inconsistencies can be eliminated and more meaningful conclusions drawn.

The reports on platelet aggregation during pregnancy are scanty and inconclusive. Some investigators found increased aggregability to ADP and adrenaline during pregnancy.[21,27,41] Our results disagree with these observations, since the aggregation responses to ADP, adrenaline, arachidonic acid, collagen, and ristocetin were significantly lower during pregnancy compared to nonpregnant controls. In contrast, other investigators could not establish any differences between pregnant and nonpregnant women.[28,42] The recently reported increase in the plasma levels of thromboxane B$_2$ and its release from thrombin-induced platelet aggregates in pregnant women suggests enhanced in vivo platelet activity during pregnancy.[43]

In conclusion, the various changes in the hemostatic variables, especially the increase in clotting factor levels, in Saudi pregnant women are similar to many previously published results and support the description of pregnancy being a "hypercoagulable state"[2,44] that assures rapid and effective hemostasis during parturition. This normal physiological situation is potentially dangerous as it increases the risk of thromboembolic disease in pregnancy, on the one hand, and of severe hemorrhage due to the development of consumption coagulopathy on the other.[1] However, the reduced platelet aggregability in Saudi pregnant women is of some interest. This state may counterbalance the raised levels of clotting factors and serve to reduce the risk of thromboembolic disease in Saudi women during pregnancy.

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INCIDENCE OF COLORECTAL CANCER AND COLONIC POLYPS IN SAUDI PATIENTS

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من بين ١٦٠٠ مريض سعودي أجري لهم التنظير الباطني في الجزء السفلي من القناة الهضمية في مستشفى القوات المسلحة بالرياض اكتشفت حالات سلائل غدية لدى ٤٠ منهم (٢,٥٠٪)، وحالات سرطان قولوني مستقيمي لدى ١٢ (٠,٧٥٪)، وداء المنشقة المنسونية لدى ١٤٩ (٩,٣١٪)، والسلائل الناجمة عن داء المنشقات لدى ٥ (٠,٣١٪) دون أن تكون مصحوبة بداء خبيث. وعلى الرغم من المعدلات المرتفعة من الاصابة بداء المنشقة المنسونية في هؤلاء المرضى إلا أنه لم يكن هنالك ارتفاع في معدلات الاصابة بسرطان القولون والمستقيم. ومن بين ١٨٤٦ مريضا سعوديا راجعوا قسم الأورام، كان ٣٤٦ منهم (١٨,٧٤٪) يعانون من داء خبيث في الجهاز الهضمي (٣٠٧ في الجزء العلوي من الجهاز الهضمي و٣٩ في الجزء السفلي من الجهاز الهضمي). إن هذا التوزيع للأورام في القناة الهضمية معاكس تقريبا لما هو سائد في الأقطار الغربية. تعتبر معدلات الاصابة بالسلائل الغدية والسرطان القولوني المستقيمي منخفضة في المملكة العربية السعودية مقارنة بالأقطار الغربية. وهذا قد يعود لعوامل وراثية وغذائية وبيئية. تؤكد الدراسة الحالية أيضا صحة نتائج الدراسات السابقة التي أجريت في مصر والتي تشير إلى أن تكاثر المنشقات المنسونية لا يلعب دورا مهما في تعرض الأمعاء الغليظة للاصابة بداء خبيث.

Of 1600 Saudi patients who underwent lower gastrointestinal tract endoscopy at the Riyadh Armed Forces Hospital, 40 (2.50%) had adenomatous polyps, 12 (0.75%) had colorectal cancer; 149 (9.31%) had *Schistosoma mansoni*, and 5 (0.31%) had schistosomal polyps but with no associated malignancy. Despite the high incidence of *S. mansoni*, there was no increase in the incidence of colorectal cancer in these patients. Of 1846 Saudi patients seen at the oncology department, 346 (18.74%) had gastrointestinal malignancy (307 in the upper gastrointestinal and 39 in the lower gastrointestinal tract). This distribution of neoplasms in the alimentary tract is almost the reverse of that seen in the West. There is a low incidence of adenomatous polyps and colorectal cancer in Saudi patients compared to the Western population. This might be due to genetic, dietary, and environmental factors. The present study also confirms previous studies from Egypt that *S. mansoni* infestation does not play a role in or predispose to large bowel malignancy.

Reports from western countries cite a high incidence of colorectal cancer compared with developing countries. We report the incidence of colonic polyps and colorectal cancer in Saudi patients seen at the gastroenterology and oncology departments of the Armed Forces Hospital, Riyadh. Both departments are major specialized centers and receive referrals from military and nonmilitary hospitals throughout Saudi Arabia.

Material and Methods

Between March 1979 and December 1985, 1775 patients (1242 males, 533 females) underwent fiberoptic sigmoidoscopy (1310 patients) or colonoscopy (465 patients) at the gastroenterology department because of different gastrointestinal problems. Saudis constituted 1600 of the patients (90.14%). This figure includes patients with polyps or tumors diagnosed initially by barium enema and who are usually referred for endo-

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scopic polypectomy or biopsy. Patients who had surgery for colorectal cancer usually had endoscopy before or after surgery for follow-up. During the endoscopic procedures, sufficient biopsies were taken from suspected lesions to allow for histologic examination. Snare polypectomy is usually done in patients with polyps, and whenever possible, polyps are completely excised.

Sigmoidoscopy is performed usually to the left flexure and colonoscopy usually to the cecum. Neither procedure is usually done as routine screening for malignancy.

In addition to the above group of patients, 2609 patients with histologically proved malignant diseases were seen at the oncology department between September 1981 and December 1985. Saudis represented 1846 of the patients (70.75%) and this number does not include any of those patients seen at the gastroenterology department.

Results

Lower gastrointestinal tract endoscopic and histologic findings from the colonic biopsies of 1600 Saudi patients showed that 40 patients (2.50%) had adenomatous polyps, five of which were multiple. *Schistosoma mansoni* ova were found in 149 patients (9.31%), and five had schistosomal polyps (Table 1).

Table 2 summarizes the findings in 12 patients with adenocarcinoma (0.72%). Their ages ranged between 32 and 62 years (mean, 49 years). Colonic biopsies in a patient who had had a renal transplant showed Kaposi's sarcoma and *S. mansoni*. *S. mansoni* was also found in the colonic biopsies from two non-Saudi patients, one with carcinoid and the other with adenocarcinoma of the rectum. The presence of *S. mansoni* was an incidental finding in these patients and histologically had no relationship to their tumors.

Of the 1846 Saudi patients seen at the oncology department, 346 (18.74%) had gastrointestinal malignancy (excluding lymphoma) and 307 (88.73%) had upper gastrointestinal malignancy, the most common of which was carcinoma of the esophagus. The remaining 39 patients (2.11%) had lower gastrointestinal malignancy (Table 3).

TABLE 1. *Polypoid lesions of large bowel diagnosed from endoscopic biopsies.*

Disease	No. of patients	% of 1600 patients	Age (yr)
Tubular adenoma	34	2.12	Range, 32-76 Mean, 48
Tubulovillous adenoma	3	0.19	Range, 41-79 Mean, 59
Villous adenoma	3	0.19	Range, 38-74 Mean, 52
Hyperplastic polyp	3	0.19	Range, 31-54 Mean, 42
Schistosomal polyp	5	0.31	Range, 28-45 Mean, 36

TABLE 2. *Malignant lesions of large bowel diagnosed from endoscopic biopsies.*

Disease	No. of patients (% 1600 patients)	Sex (M:F)	Age (yr)
Adenocarcinoma in colon	10 (0.60%)	4:6	Range, 32-62 Mean, 48
Adenocarcinoma in rectum	2 (0.12%)	2:0	Range, 50-62 Mean, 55
Kaposi sarcoma (+ schistosomiasis)	1 (0.06%)	0:1	33

TABLE 3. *Saudi patients with lower gastrointestinal tract malignancy seen in the oncology department.*

Disease	No. of patients	Sex (M:F)	Age (yr)
Adenocarcinoma in colon	16	11:5	Range, 18-80 Mean, 47
Adenocarcinoma in rectum	16	10:6	Range, 18-80 Mean, 52
Squamous cell carcinoma in anal canal	6	3:3	Range, 47-60 Mean, 56
Adenocarcinoma in anal canal	1	1:0	34

Discussion

This study has shown that the incidence of colorectal cancer and polyps is low in Saudi patients compared with the Western population, and that the distribution of malignancy in the alimentary tract is almost the reverse of that encountered in the West. In Saudis, malignancy of the upper gastrointestinal tract is more common than that of the lower gastrointestinal tract. Of the patients with gastrointestinal malignancy seen at the oncology department, 88.73% had upper gastrointestinal tract malignancy while only 11.27% had malignancy of the lower gastrointestinal tract. This has also been shown in previous studies of cancer in Saudi Arabia.[1,2] El-Akkad[3] studied 1696 patients with cancer; of these only 49 patients (2.9%) had colorectal cancer compared with 113 (6.7%) with carcinoma of the esophagus and 63 (3.7%) with carcinoma of the stomach.

In the present series, colon cancer was more common in younger age groups than is seen in the Western population.[4,5] Colorectal cancer is the most common gastrointestinal malignancy in Western countries.[4] A review of over 5000 autopsies done over 35 years in an American population showed that the prevalence of colonic adenomatous polyps has ranged from 9.5 to 61% (mean, 29.5%).[5]

Recent evidence relates two groups of nutrients–fat and fiber—to colon cancer. A high-fiber diet reduces the incidence of colonic malignancy while an increased intake of dietary fat promotes cancer.[6,7] The low incidence of colorectal cancer in Saudis may be related to several factors, including environment, heredity, and diet. The usual Saudi diet consists of cereals, high-fiber products, and Laban (yogurt). There is also a low incidence of the precursors to large bowel carcinoma, such as adenomatous polyps, familial polyposis coli, Gardner's syndrome, and ulcerative colitis.

The incidence of colorectal cancer is also low in other Middle Eastern countries compared to the West. Dajani et al[8] reported the incidence rates in Jordanians as 0.5 (colon) and 0.6 (rectum) per 100,000 general population compared to 27 (colon) and 12 (rectum) per 100,000 in Nova Scotia, Canada. Cancer of the colon constitutes only 0.9% of the cancer in Iraq.[9] A similar low incidence has also been reported from Kuwait[10] and Lebanon.[11]

Our study also confirms findings from previous reports from Egypt that *S. mansoni* infestation does not predispose to colorectal cancer. In 9.31% of our patients, *S. mansoni* was diagnosed from biopsies of the colon or rectum, and there were no dysplastic changes noted in five patients with schistosomal polyps and no association has been noted between the *S. mansoni* and malignancy.

Schistosomiasis is endemic in Saudi Arabia,[12] and a high incidence of colorectal cancer would therefore be expected if *S. mansoni* predisposed to malignancy.

Although there may be an association between *S. haematobium* and carcinoma of the bladder,[13] and *S. japonicum* and bowel malignancy,[14] no such association has been established with *S. mansoni*. Dimette et al[15] studied 98 Egyptian patients with carcinoma of the large bowel; 17 had *S. mansoni* infestation. Detailed histologic studies revealed no outstanding features that distinguished the parasitic from the nonparasitic group. This has also been documented in another large series from Egypt.[16] In these series, no malignant transformation of schistosomal polyps has been established.

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CARCINOMA OF THE RECTUM AT KING FAISAL SPECIALIST HOSPITAL: A FOUR-YEAR RETROSPECTIVE REVIEW

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أجريت دراسة مراجعة على مائة واثنين مريضا (٣٤ انثى و٦٨ ذكرا) ممن يعانون من ورم سرطاني في المستقيم على مدى أربع سنوات (١٩٨٤ـ١٩٨٧م). تبين أن المعدل النسبي للاصابة السنوية يتراوح ما بين ١,٥ إلى ١,٩٪ ومتوسط العمر ٥٤,٨ عاما (الأدنى ١٥ والأقصى ٩٦) مع ارتفاع معدلات الحدوث لدى المرضى الأصغر سنا (نسبة ٢١,٥٪ ما دون الأربعين). كان من السمات المألوفة لهذه الحالات (نسبة ٤٦٪ لا تصلح للجراحة عند العرض). تأخر العرض على الطبيب. رفض العلاج ١٣ مريضا (نسبة ٢٣,٦٪ من الآفات المناسبة للجراحة) لأنهم لم يقبلوا فغر القولون.

كان اثنان وأربعون من الأورام المستأصلة (نسبة ٥٤,٨٪) من نوع آفة ديوك، وكانت السرطانة الوسفية المخاطية كثيرة التوارد بدرجة ملحوظة (نسبة ١٩ و٩,٥٪ على التوالي)، وحدث ٣٥ ورما (٨٣,٣٪) ضمن مسافة ثمانية سنتيمترات من حافة الشرج. وثبتت معاودة الاصابة لدى ستة عشر مريضا (٣٨٪) (متوسط زمن المتابعة، ١٤,٤ شهرا). وظهر أن معدلات المعاودة مشابهة لما ظهر في التقارير الأخرى، بخاصة عند تحليل الحالات وفقا لمراحل ديوك. إن عدم تقيد المرضى بتعليمات العلاج والمتابعة قد أحدث مشكلات كبرى بالنسبة للعلاج السريري للداء وتفسير النتائج. تشير الدراسة الحالية إلى أهمية التركيز على زيادة معدلات التعليم الصحي وبث الوعي للالمام بمخاطر هذا الداء. وتوصي بإجراء فحص جماعي لتحديد حجم المشكلة للتوصل إلى تشخيص مبكر للحالة. وينبغي توفير الأجهزة المساندة لعملية فغر القولون لمساعدة المرضى على قبول هذه المعالجة التي قد يكون فيها الشفاء.

One hundred and two patients (34 females, 68 males) with rectal carcinoma were the subject of a retrospective review conducted over a four-year period (1984-1987, inclusive). An annual relative incidence of 1.5 to 1.9%, mean age of 54.8 years (minimum 15, maximum 96), and a high incidence in young patients (21.5% below age 40) were found. Late presentation was common (46% inoperable on presentation). Thirteen patients (23.6% of operable lesions) refused treatment because they would not accept colostomy. Of the resected tumors (N = 42), 54.8% were Duke's C lesions; mucoid and squamous cell carcinoma were significantly frequent (19% and 9.5%, respectively); and 35 tumors (83.3%) occurred within 8 cm of the anal verge. Sixteen recurrences (38%) were documented (mean follow-up, 14.4 months). Recurrence rates were comparable to those given in other reports, especially when the cases were analyzed according to Duke's stages. Failure of patients to comply with treatment and follow-up posed major problems in the clinical management of the disease and in interpreting results. The present study emphasizes the need for increased health education and awareness of this disease. Mass screening is suggested to define the size of the problem and aid in early diagnosis. Supportive facilities for colostomy are needed to help patients accept a potentially curable treatment.

Carcinoma of the rectum is one of the most common malignant diseases in the West, second to lung cancer in males and third to breast and lung cancer in females. Factors related to the western environment, mainly diet and heredity, are believed to be major influences in the develop-

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ment of this cancer. It is usually believed that in societies such as Saudi Arabia, where the lifestyle is natural, such tumors are rare or at least uncommon. It is our impression, however, that carcinoma of the rectum occurs more frequently than expected, with many cases presenting late in incurable stages, and that a significant number of young patients are affected. A large number of patients refuse treatment because they will not accept a permanent colostomy.

The purpose of this retrospective review was to determine the preliminary epidemiologic and pathologic features of this tumor in the local environment; to review the patterns of presentation and problems encountered with diagnosis and management; and to present the operative strategy and outcome in terms of recurrence, compared to current international standards.

Patients and Methods

The cases of 102 patients (34 females, 68 males) with carcinoma of the rectum who presented at King Faisal Specialist Hospital over a four-year period (1984-1987, inclusive) were retrospectively reviewed. Mean age was 54.8 years (minimum 15, maximum 96). Non-Saudis were excluded. History, operative and pathologic reports, and follow-up documentation were reviewed, and the data obtained were grouped and analyzed.

Carcinoma of the rectum was defined as all malignant tumors of the distal large bowel shown by colonoscopy to lie within 15 cm from the anal verge, or found at laparotomy to lie at or below the rectosigmoid junction.

Results

Of the 102 Saudi patients who made up the study, 22 (21.5%) were below the age of 40 and 11 (10.7%) were under 30. The annual incidence of the tumor ranged between 1.3 and 1.9% of all primary malignant tumors seen at our institution (Table 1). The most common presentations in decreasing frequency were: rectal bleeding (61%), pain (perineal or abdominal) (29.4%), and change in bowel habit (27.4%); intestinal obstruction constituted only 5.9% of all presentations (Table 2).

TABLE 1. *Incidence.**

Year	Incidence (%)	Cancer of rectum/all primary malignancies
1984	1.9	31/1581
1985	1.7	27/1529
1986	1.3	24/1762
1987	1.5	33/2121

*Information from KFSH&RC Tumor Registry, 1987.[3] (Figures include non-Saudis.)

TABLE 2. *Symptomatology.*

Symptom	Distribution of patients according to duration of symptoms				Total no. of patients
	<3 mo	3–6 mo	6-12 mo	>12 mo	
Bleeding					
Alone	1	4	5	18	
With other symptoms	1	9	8	16	62
Pain					
Alone	2	3	2	1	
With other symptoms	1	9	6	6	30
Bowel irregularity					
Alone	3	2	4	–	
With other symptoms	–	6	5	8	28
Intestinal obstruction					
Alone	2	1	–	–	
With other symptoms	–	1	2	–	6

One third (35%) of all patients had had symptoms for more than 12 months; of these, 6 patients sought medical advice at least several months before diagnosis was made. Two of the six patients underwent hemorrhoidectomy in other hospitals.

Only 55 patients had operable tumors on presentation, two of whom were found to have liver metastasis at the time of resection (Duke's Stage D) that was not detected on preoperative computed tomographic (CT) scans. Of these 55 patients, 13 refused operation because they would not accept colostomy. Of the 47 patients with inoperable tumors, 31 had advanced local or distant disease (15 were given palliative colostomy), 9 presented with recurrence after primary resection done at another institution, and 7 patients were denied surgery because of their poor general condition.

The type of operative procedures and the histologic variants for the 42 operable lesions are shown in Table 3. Twenty-five patients had abdominoperineal resection, 15 had sphincter-saving procedures (12 were anterior resections, and three abdominosacral resections), and two patients had local excisions.

Adenocarcinoma, including the mucinous variant, was the most common pathologic type (85%). Mucinous adenocarcinoma and squamous cell carcinoma were relatively frequent and represented 19% and 9.5%, respectively, of all the cases of rectal cancer.

The sites of the operable lesions in relation to the distance from the anal verge and the operative procedures performed are summarized in Table 4. Local recurrence detected within the follow-up period is also included. Twenty-six tumors were within 5 cm of the anal verge; three patients had a sphincter-saving procedure with one local recurrence and two had local excision with no recurrence. Nine lesions were between 5 and 8 cm of the anal verge; 5 patients underwent a sphincter-saving procedure with no recurrence. There were five lesions located in the middle third (8-12 cm); all patients were treated with a sphincter-saving procedure, with two subsequent local recurrences. Only two lesions occurred in the upper third (12-15 cm) of the rectum; both were treated with a sphincter-saving resection, with no local recurrence.

TABLE 3. *Operative procedures and histologic types.*

		Histology			
Procedure	Total	Adeno	Mucinous	Squamous	Other
APR	25	14	6	4	melanoma (1)
AR	12	10	1	–	carcinoid (1)
ASR	3	3	–	–	–
Local excision	2	1	1	–	–
Total	42	28	8	4	2

APR = abdominoperineal resection; AR = anterior resection; ASR = abdominosacral resection.

TABLE 4. *Height of lesions, operative procedures, and local recurrence.*

	0–<5 cm		5–<8 cm		Middle third 8–<12 cm		Upper third 12–15 cm	
Procedure	Total no.	Local recurrence	Total no.	Local recurrence	Total no.	Local recurrence	Total no.	Local recurrence
APR	21	3	4	1	0	–	0	–
AR	2	0	3	0	5	2	2	0
ASR	1	1	2	0	0	–	0	–
Local excision	2	0	0	–	0	–	0	–
Total	26	4	9	1	5	2	2	0

APR = abdominoperineal resection; AR = anterior resection; ASR = abdominosacral resection.

Follow-up was not regular because of compliance failure by patients. The mean follow-up period was 14.4 (range, 6-42) months. Only one patient died in the immediate postoperative period (within 28 days) as a result of anastomotic leak leading to severe local and systemic sepsis. There were 16 recurrences: eight perineal and eight systemic. Classification of these recurrent cases according to Duke's staging is shown in Table 5. The incidence of C lesions was 54.8%, and more Stage C than B lesions were seen in patients who had sphincter-saving operations, compared to those who had abdominoperineal resection.

Discussion

Carcinoma of the rectum is the most common visceral malignancy occurring in the Western population and is the cause of a large number of deaths per year, according to studies from Europe and North America.[1,2,10,13,14] Factors responsible for its high incidence in the West include diet, heredity, inflammatory bowel diseases such as ulcerative colitis, and more importantly, untreated benign adenomas.

It is commonly believed that carcinoma of the large bowel is rare in the populace of environments such as Saudi Arabia, where the lifestyle is more natural. However, this lifestyle is rapidly becoming more westernized, especially as increas-

TABLE 5. *Recurrences according to Duke's classification.*

	Operations					Recurrences					
		Duke's stage					According to site		According to stage		
Procedure	Total	A	B	C	D	Total	Perineal	Systemic	B	C	D
APR	25	0	10	14	1	8	5	3	2	5	1
AR/ASR	15	1	4	9	1	8	3	5	1	6	1
Local excision	2	0	2	0	0	0	0	0	0	0	0
Total	42	1	16	23	2	16	8	8	3	11	2

APR = abdominoperineal resection; AR = anterior resection; ASR = abdominosacral resection.

ing numbers of rural dwellers move to more urban areas.

In the present study, carcinoma of the rectum constituted an annual incidence of 1.5 to 1.9% of all primary malignant tumors seen (Table 1).[3] The most common types of tumors seen at our institution and their relative incidence are shown in Table 6. Although the number of rectal carcinomas seen in our hospital could be increased over those seen at other hospitals in the Kingdom, most other oncologic cases are also referred to this hospital. Accordingly, the relative frequency of this tumor in our hospital is probably indicative of its occurrence throughout the Kingdom. Unfortunately, no tumor statistics are available in Saudi Arabia, but our supposition can be supported by information published by the World Health Organization[4] on the incidence of carcinoma of the rectum in neighboring countries. The relative incidence of this tumor in relation to all malignant tumors was found to be between 1 and 2% in Kuwait, Iraq, and Iran; the sex ratio was similar for all three areas (see Table 7).

The female-to-male ratio in our study was nearly 1:2; there was a slightly greater male preponderance in our patient population compared to ratios reported in other series.[1,2,5-7] The mean age of patients in our study (54.8 years) was somewhat lower than that reported in other series (60-70 years),[2,5,6] which reflects the high incidence of this tumor in young patients (21.5% and 10.7% for ages below 40 and 30, respectively). These are strikingly high figures compared to those published by Martin et al,[8] Bedikian et al,[9] and Okuno et al[5] who reported incidences of rectal cancer in patients below 40 years of age of 3.5%, 7%, and 10%, respectively.

TABLE 6. *Relative incidence of the most common malignant tumors at King Faisal Specialist Hospital and Research Centre (all ages and all nationalities).**

Tumors	Total no. (%)	Males	Females
All primary malignant tumors	2121	1121	1000
Leukemias	175(8.25)	102	73
Lymphomas–non-Hodgkin's	130(6.13)	94	36
Lymphomas–Hodgkin's	62(2.92)	44	18
Breast	173(8.15)	2	171
Central nervous system	138(6.50)	67	71
Thyroid	129(6.08)	31	98
Oral cavity	110(5.18)	60	50
Lung	86(4.05)	63	23
Esophagus	78(3.67)	50	28
Bladder	78(3.67)	56	22
Visceral (stomach, liver, pancreas, and colorectal)	272(12.82)	180	92
Rectum alone	33(1.55)	19	14

*Information from KFSH&RC Tumor Registry 1987.[3]

TABLE 7. *Incidence of carcinoma of the rectum in neighboring countries.**

	Total no. of all malignancies	No. of cancer of rectum cases	Males	Females
Kuwait (1974–1978)	808	9(1.11%)	6	3
Iraq (1976–1982)	24,101	393(1.63%)	242	151
Iran (1981–1982)	7,247	150(2.0%)	85	65

*Information from WHO publication.[14]

The tumor type in the majority of the operable cases, as expected, was adenocarcinoma (85.7%). However, the incidences of the aggressive mucinous and squamous cell carcinomas were relatively high−19 and 9.5%, respectively. Okuno et al[5] reported a 7% occurrence of mucinous adenocarcinoma, while cases of squamous cell carcinoma were very uncommon (0.6%).

Based on the distance from the anal verge (Table 4), most tumors (35/42) were located in the lower third of the rectum and anal canal. In most other series, tumors were more frequently located in the upper third and rectosigmoid junction.[1,7,10] Low rectal tumors have, in general, a worse prognosis, and with the distribution observed in our series, a poor outcome would be expected, especially considering the high incidence of aggressive mucinous adenocarcinoma and squamous cell carcinoma.

One of the major problems in the management of this and other malignant diseases in a country such as Saudi Arabia is related to the inadequate health education and lack of public awareness of the warning signs of cancer. A major problem is late presentation: 35% of our patients had had symptoms for more than 12 months, with the result that the number of incurable cases was extremely high (46%). In the St. Mark's Hospital study,[1] only 6.8% of the patients had inoperable tumors but this hospital is a referral center and the patients are somewhat selected. A more representative figure is provided by the study of Moran et al[11] which revealed an 18.4% incidence of inoperable cases.

The problem of late presentation is, however, not entirely due to patients' delay. In our series, two patients had had hemorrhoidectomy several months before they were referred to us. There must also be increased awareness of rectal cancer on the part of medical practitioners. This issue has been stressed even in societies with high health care standards such as Britain.[12] Increased knowledge of the etiologic factors relating to the environment will heighten awareness of the disease. The higher incidence in young people, in tumors near the anal verge, and in aggressive histologic types indicates that the causes are not necessarily identical to those in Western countries.

Screening of asymptomatic patients is needed both to elucidate the epidemiologic factors and to aid in early diagnosis. Routine digital examination, fecal occult blood testing (hemoccult test), and colonoscopy are the recommended methods.

In spite of the fact that the yield from mass screening with the simple hemoccult test is small (positive in 1.5-3.3% and one carcinoma detected in every 3,000 to 6,000 asymptomatic subjects)[14,15] and that the cost effectiveness can be high, especially if benign anorectal disease is common, this test remains the most useful screening aid.[14,15] Johnson and Jolly[13] found that the cost per carcinoma detected, using mass screening with hemoccult testing, was approximately $10,000 (U.S.).

Lack of patient compliance during treatment and follow-up is another problem encountered in our population. Many patients miss follow-up visits and, accordingly, survival rates cannot be assessed. Recurrence rates are also underestimated, but this is common to most studies because many asymptomatic recurrences can be easily overlooked.

Another problem is patients' attitude toward colostomy. In our series, 13 patients (23.6% of operable cases) refused potentially curable surgery because they could not accept the idea of colostomy. A tremendous effort was made to acquaint these patients with the purpose and functioning of a colostomy, and for those who accepted it, more effort was spent afterwards. Fear of colostomy malfunction, personal embarrassment, and other social circumstances lead to refusal of surgery. Such anxiety can be alleviated with the help of experienced colostomy nurses and an understanding physician, and the involvement of patients who have undergone colostomy.

Outcome of treatment is of course affected by the difficulties encountered in the management of these patients. Tumor behavior, its aggressiveness, and the adequacy of surgical resection are the major factors determining survival and recurrence. Unfortunately, because of the retrospective nature of our study, the results in this respect cannot be fully assessed. Because of the problems with inadequate follow-up, accuracy of documentation cannot be claimed. Accordingly, it might be predicted that recurrence rates are higher than those reported. Only a prospective study with rigid diagnostic, operative, and follow-up criteria can yield meaningful conclusions, especially in establishing the prognostic trend of these tumors.

The systemic and local recurrences documented in our patients are shown in Table 5 and the overall recurrence rate versus those from various other

TABLE 8. *Recurrence rates.*

Study	Overall recurrence	Recurrence according to Duke's Stage	
		B	C
This study	16/42(38%)	3/16(18.7%)	11/23(47.8%)
Williams & Johnston[16]	53/154(34.4%)	12/58(20.7%)	36/68(52.9%)
Wolmark & Fisher[18]	173/413(41.9%)	39/146(26.7%)	134/267(50.2%)
Neville et al[10]	156/373(41.8%)	20/154(13.0%)	46/126(36.5%)*
Localio et al[17]	49/360(13.6%)	18/135(13.3%)	28/111(25.2%)*

Local recurrence only.

reports is given in Table 8. However, as noted previously, the true recurrence rates might be higher than those reported. There were also a large number of Duke's C lesions in the tumors in our series (23/42), which reflects late presentation. Two patients were found at laparotomy to have liver metastasis (Stage D) not previously detected on preoperative CT scans (Table 5). Further analysis of the recurrence rates, based on Duke's staging, shows that the rates for Duke's B and C lesions are comparable to those reported elsewhere (Table 8).

Comparison between lesions treated with sphincter-saving procedures and those treated with abdominoperineal resection shows a higher number of recurrences in the group with sphincter-saving resection (Table 5). However, there was a high proportion of Duke's C to B lesions in the sphincter-saving resection group compared to the abdominoperineal resection (9C/4B versus 14C/10B, respectively) that could account for this finding. Also, two patients in the sphincter-saving resection group refused abdominoperineal resection for their low rectal tumors. They accepted the risk of recurrence rather than having a colostomy. One patient had local recurrence and the other developed systemic recurrence, both within 12 months of surgery.

Conclusion

Rectal cancer is not as uncommon in Saudi Arabia as has been believed, and the incidence could well be increasing, especially since the lifestyle is rapidly becoming more westernized. There is a particularly high incidence in young people and for pathologically aggressive tumors. Long-term prognosis cannot be deduced from the present data, but the results of treatment in terms of recurrence are comparable to those reported elsewhere.

Health education, especially of the warning signs of cancer, and increased awareness of the seriousness of the disease, both among the lay public and medical practitioners, are essential for early diagnosis. More supportive facilities are needed to enable patients who require abdominoperineal resections and permanent colostomies to cope with the practical aspects of colostomy care and overcome the cultural barriers as well. To significantly reduce the number of late-presenting cases of rectal tumors, mass screening tests should be implemented. This would, at least, aid in the detection of populations at special risk, and help establish the epidemiologic factors involved. A prospective well-controlled study is also needed to establish the influence of surgical treatment on the prognosis for patients with rectal cancer.

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LARYNGOTRACHEOBRONCHIAL FOREIGN BODIES

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أجريت دراسة مراجعة على ست وأربعين حالة رشف لأجسام غريبة خلال الفترة من ١ المحرم ١٤٠١هـ إلى ٣٠ ذي الحجة ١٤٠٨هـ (٨ نوفمبر ١٩٨٠م ـ ١٢ أغسطس ١٩٨٨م) في مستشفى الملك فهد بالهفوف بالاحساء، المملكة العربية السعودية. كان معظم المرضى دون الثانية عشر من العمر (عدد = ٤٣ نسبة ٩٣٪) في حين أن نسبة الاصابة بلغت ذروتها بين السنة الأولى والثالثة من العمر (١٩ حالة (نسبة ٤١٪). تفوقت نسبة الذكور على الاناث بدرجة طفيفة (٢٥ حالة، نسبة ٥٤٪). لوحظت أعراض وعلامات جسدية لدى أربعين مريضا (نسبة ٨٧٪) بينما ظهرت لدى ١٤ مريضا (نسبة ٤ , ٣٠٪) علامات على صورة الصدر بالأشعة السينية. تم نزع الأجسام الصلبة من المرضى بالتنظير القصبي بالمنظار الصلب تحت التخدير العام. ينبغي اللجوء إلى التنظير القصبي عندما يوحي تاريخ الحالة بارتشاف جسم غريب وإن لم تظهر دلائل إشعاعية هامة أو حينما تشير نتائج الفحص الطبي إلى حدوث ارتشاف جسم غريب حتى في غياب القصة المرضية.

A retrospective review was conducted on 46 cases of foreign body aspiration seen during 1 Muharram 1401H (8 November 1980) to 30 Dhu Al-Hijjah 1408H (12 August 1988) at the King Fahad Hofuf Hospital, Al-Hassa, Kingdom of Saudi Arabia. The majority of patients (N = 43; 93%) were under 12 years of age with a peak incidence of 19 cases (41%) occurring at 1 to 3 years of age. There was only a slight male preponderance of 25 (54%) cases. Abnormal physical signs and symptoms were seen in 40 patients (87%), while 14 (30.4%) showed abnormal chest x-ray findings. The foreign bodies were removed through a rigid bronchoscope with patients under general anesthesia. Bronchoscopy should be done when the history is suggestive of aspiration even in the absence of significant abnormal radiographic findings, and when abnormal physical findings suggest aspiration even with an otherwise negative history.

The problem of foreign body aspiration has long been recognized. As early as 1690, Muys recorded a case of death by suffocation in a 7-year-old child three months after inhalation of a bean.[1] In 1897, Killian was the first to remove a foreign body using a hollow tube.[1] Despite improved anesthetic and bronchoscopic techniques, foreign body aspiration still remains the principal cause of death at home in children under 6 years of age.[2]

We will discuss the usual clinical manifestations and risk factors in our cases, and will describe our method of endoscopic removal of aspirated foreign bodies. Cases with unusual presentations and their management are also discussed.

Material and Methods

The medical charts at the King Fahad Hofuf Hospital (KFHH) coded for transpharyngeal esophageal and airway foreign bodies were reviewed. Forty-six patients with laryngotracheobronchial foreign bodies who underwent laryngotracheal bronchoscopic removal constituted the study population. All were in the pediatric age group (< 12 years) except for three; the oldest was 18 years. Of the 43 (93%) patients under the age of 12 years, 30 (70%) were younger than 3 (Table 1). There were 25 (54%) males and 21 (46%) females. Presenting signs included: dyspnea, 25; paroxysmal cough, 13; wheezing, 10; fever, 4; stridor, 4; cyanosis, 3; and choking, 3. Twenty-two patients had two or more signs and symptoms and six patients had no symptoms.

The main abnormal auscultatory finding was decreased breath sounds in 9 (20%) patients.

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Radiographic diagnostic procedures consisted mainly of chest x-ray studies in the anteroposterior and lateral positions during inspiratory and expiratory phases. The majority of the patients (N = 32; 69.5%) had normal chest x-ray studies. A radiopaque foreign body was demonstrated in 7 cases (15.2%). Inspiratory-expiratory mediastinal shift, hyperinflation of a lung, and pneumonia occurred in 4 cases (8.7%) each.

The time that elapsed between aspiration and removal of the foreign bodies varied widely among the patients, ranging from less than six hours to about two years.

In all 46 cases, the decision to do bronchoscopy was made by the ENT surgeon in consultation with the pediatrician or attending physician. A definite history of foreign body inhalation was elicited in 42 (91%). Those patients who did not have a definite history underwent bronchoscopy if clinical findings from physical examination and x-ray studies suggested the presence of a foreign body, and if there were repeated episodes of chest infection.

A fiberoptically lighted rigid bronchoscope (WOLF), ranging in size from 3 × 160 mm to 8 × 400 mm with diameters in 0.5-mm increments, was selected according to the patient's age and was generally used with a Jackson-type pediatric foreign body forceps.

A proximal magnifying lens was used when necessary for better visualization. All procedures were performed with the patient under inhalation anesthesia through the side gas line of the bronchoscope. In most cases, varying amounts of steroids were given perioperatively as prophylaxis against postoperative edema. Antibiotics, mucolytics, oxygen, and steam inhalation were generally administered after bronchoscopy.

The majority of foreign bodies recovered were organic (N = 32; 70%) and included mainly seeds from watermelons, sunflowers, or pumpkins, as well as peanuts and a variety of vegetable seeds and seed shells. Inorganic foreign bodies consisted of a plastic nozzle, plastic pieces from toys, metallic pieces, pins, and safety pins (Table 2).

The foreign bodies were lodged most often in the right main bronchus (N = 25; 54.3%). The rest were in the trachea (N = 9; 19.5%); left main bronchus (N = 8; 17.4%); larynx (N = 3; 6.5%); and right lower segmental bronchus (N = 1; 2%).

TABLE 1. *Age distribution.*

Age (y)	No.(%)
0 – 1	11(24)
2 – 3	19(41)
4 – 6	7(15)
7 – 12	6(13)
Above 12 years	3(7)

TABLE 2. *Type of foreign body.*

Foreign body	No. of patients
Organic	
Watermelon seeds	8
Vegetable seeds	8
Sunflower seeds	5
Shells of different seeds	4
Peanuts	3
Pumpkin seeds	1
Carrot	1
Orange peel	1
Fish bone	1
Total	32
Inorganic	
Plastic nozzle	6
Other plastic pieces	4
Metal pieces	1
Cellophane	1
Pin	1
Safety pin	1
Total	14

Unusual Cases

Patient 1

An 18-year-old Saudi female came to the KFHH emergency room after having inhaled a pin while mending clothes an hour before admission. She was experiencing no chest pain, cough, dyspnea, or other symptoms. Auscultation showed no abnormality. A plain chest x-ray study showed an inverted pin in the right lower segmental bronchus. She was subsequently admitted for possible bronchoscopy and removal of the foreign body under general anesthesia. Four hours after admission, after no oral intake of food or fluids, she had a sudden bout of coughing and expelled the pin, as verified later by chest x-ray study.

Patient 2

A 7-year-old male Saudi child was admitted through the KFHH emergency room for asthma-like symptoms consisting of dyspnea and wheezing. He had had other similar attacks that were treated outside of the hospital and relieved by medications for bronchial asthma. There was no recent history of foreign body aspiration. Plain chest and neck x-ray studies showed an inverted open safety pin in the larynx just below the vocal cords. Upon further questioning, his elder brother recalled that the patient might have aspirated the pin about 2 years back, when a safety pin the child was playing with disappeared from his mouth. Because of the location of the foreign body, initial inhalation anesthesia was administered by mask. Direct laryngoscopy showed a rusty, inverted, open safety pin with tips embedded crosswise below the vocal cords. Because of the possible breakage of the foreign body and the prolonged general anesthesia needed for a difficult removal by direct laryngoscopy, a tracheostomy was done instead. With a long curved arterial forceps, the base of the safety pin was grasped through the tracheostomy and successfully extracted. He was weaned off the tracheostomy tube and discharged from the hospital within five days.

Patient 3

A 3-year-old male Saudi child came to the KFHH emergency room because of cough, fever, and dyspnea that had been unrelieved by oral medications prescribed by a private physician. On admission the child was highly febrile (39.5°C). Auscultation revealed crepitant rales and wheezing in the left lung field. The chest x-ray appearance was a left lobar pneumonia. Under parenteral penicillin, and other medications, his symptoms abated, and the chest sounds cleared; the patient was discharged from the hospital after seven days.

Over a month later, the patient returned to the Pediatric Outpatient Clinic with the same complaints of cough, fever, and dyspnea. He had crepitations and wheezing in the left lung field. Repeat chest x-ray study showed atelectasis of the left lung, mediastinal shift to the left, and right-sided hyperaeration. He was readmitted by the pediatrician, and after conservative management with antibiotics, mucolytics, expectorants, oxygen inhalation, and physiotherapy, which failed to re-expand the left lung, the ENT surgeon was consulted. Bronchoscopy under general anesthesia revealed an edematous left main bronchus filled with copious mucopurulent discharge. After suctioning out the infected material, a 1 × 2 cm cellophane biscuit wrapper was seen and extracted. The patient recovered completely and was discharged from the hospital.

Discussion

Our review confirms the findings of others that the highest incidence of foreign body aspiration occurs in children younger than 3 years. At this age, children are unable to chew edibles adequately. In addition, inert nonchewable objects are often placed in the mouth and can be aspirated easily, especially while the child is running, playing, or talking.[3]

Although other reports confirm the 2:1 male to female ratio in children,[3] our data suggest a slight male preponderance.

The most common signs and symptoms of dyspnea or shortness of breath, cough, wheezing, and decreased breath sounds were seen in the majority of cases (40/46; 87%). Radiographic findings were often not very helpful. This is perhaps due to the difficulty in coordinating inspiratory and expiratory films. It has therefore been suggested that fluoroscopy is the preferred diagnostic method. However, even fluoroscopy has not been uniformly helpful, yielding false negative results in up to 45% of cases.[3]

Most of the foreign bodies encountered were organic in origin and consisted mainly of a variety of seeds. Unlike Western countries where peanuts are the most commonly encountered foreign body, our findings agree with those of Ashoor et al[4] who found that in the Middle East watermelon seeds are the most common foreign body. The most common inorganic foreign body encountered has proved to be the plastic nozzle. This black cylindrical plastic whistle comes from rubber toy balloons. The sale of this toy should be prohibited because of the danger it poses.

Most of the foreign bodies were lodged in the right mainstem bronchus. This finding agrees with the initial findings of Jackson and Jackson from over thirty years ago, who observed that this is probably due to several reasons: the right main bronchus's greater diameter, its lesser angle of deviation from the tracheal axis, the action of the trachealis muscle, the greater volume of air entering the right lung on inspiration, and the position of the carina, which is usually to the left of the midline. Lowe and Russell[5] reported that the position of the carina is the main reason for this. A significant number of foreign bodies in our cases were also found in the trachea, left mainstem bronchus, larynx, and right segmental bronchus. It is therefore mandatory that bronchoscopy include all these areas.

The three unusual cases are presented to illustrate three points. (1) A foreign body may be inhaled without resultant abnormal signs and symptoms (Patient 1). (2) A patient may present with multiple abnormal signs and symptoms such as cough, fever, and dyspnea with or without radiographic findings of hyperaeration, mediastinal shift, and atelectasis, even in the absence of a history of foreign body aspiration (Patient 3). (3) An alternative route of foreign body extraction should be considered in cases of impaction when transglottic removal is deemed impossible or too dangerous. These three cases prove the point that "All is not asthma that wheezes." Asthmatoid wheezing heard at the open mouth is an important sign of a foreign body lodged in the trachea or large bronchus. This symptom in a child is always suggestive of foreign body, and if it persists after paroxysmal coughing, this is diagnostic.[6]

The decision to do bronchoscopy in a patient with suspected foreign body aspiration is based on a suggestive history and the presence of abnormal signs and symptoms as well as abnormal radiographic findings. In no instance should it be ruled out in the absence of one finding or another.

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CHRONIC INTERMITTENT PERITONEAL DIALYSIS USING AUTOMATIC CYCLER MACHINE

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على الرغم من وجود مراكز عديدة للديال الدموي في المملكة العربية السعودية ، إلا أن عددا قليلا جدا منها يلجأ إلى الديال الصفاقي المزمن . نصف في هذه المقالة مشاهداتنا في دراسة مدتها سبع سنوات أجريت على ٢٨ مريضا مصابين بداء الكلى النهائي ، وتم تدبير حالاتهم بالديال الصفاقي المتقطع المزمن باستخدام جهاز آلي دوري وذلك من مستشفى الهدا العسكري بالطائف . تراوحت مدة الديال بين أربعة أشهر و٦٠ شهرا وأما أعمار المرضى فقد تراوحت بين ستة أعوام و٧٤ عاما . كانت مبررات اختيار الديال الصفاقي بدلا عن الديال الدموي وجود داء قلبي وعائي شديد أو نزف مخي أو نزف شبكي أو غياب المنفذ الوعائي المناسب . وقد تم تقييم هذه الطريقة واختلاطاتها ومآل المرضى فتبين ضآلة نسبة وقوع التهاب الصفاق إيجابي الزرع بمعدل ٠٫٤٨٪ حادثة لكل مريض/ سنة . ظل سبعة مرضى على برنامج الديال الصفاقي المتقطع المزمن، وأجريت لخمسة مرضى عملية نقل الكلية، وتحسن الأداء الوظيفي للكلى لدى اثنين، ونقل ثلاثة مرضى إلى مستشفيات أخرى، وتحول مريضان إلى الديال الدموي باختيارهم وتوفي تسعة مرضى . نخلص إلى القول بضرورة إدخال الديال الصفاقي كبديل لدى مرضى داء الكلى النهائي الذين يعانون من مرض قلبي وعائي شديد أو من لا يوجد لديهم منفذ وعائي مناسب . وفي حالة عدم توفر الديال الصفاقي الجوال أو الديال الصفاقي الدوري المزمن، فإنه يمكن بسهولة تبني طريقة الديال الصفاقي المتقطع المزمن في معظم وحدات معالجة أمراض الكلى .

Although there are many hemodialysis centers in Saudi Arabia, only a few offer chronic peritoneal dialysis. We describe our findings from a 7-year study of 28 patients with end-stage renal disease who were maintained on chronic intermittent peritoneal dialysis (CIPD) using automatic cycler machines located at Al-Hada Armed Forces Hospital, Taif. The duration of dialysis ranged from 4 to 60 months and the age of the patients ranged from 6 to 74 years. The indications for choosing peritoneal dialysis rather than hemodialysis included severe cardiovascular disease, cerebral hemorrhage, retinal hemorrhage, and lack of vascular access. The technique, complications, and outcome of patients were evaluated. The incidence of culture-positive peritonitis was low at 0.48 episodes per patient year. Seven patients remain on CIPD, five have undergone kidney transplants, kidney function improved in two, three were transferred to other hospitals, two were switched voluntarily to hemodialysis, and nine died. Patients with end-stage renal disease who have severe cardiovascular disease and those with poor vascular access should be offered the alternative of peritoneal dialysis. If chronic ambulatory peritoneal dialysis or chronic cyclic peritoneal dialysis is not feasible, then CIPD as described can be adopted easily in most nephrology units.

Although chronic peritoneal dialysis in its various forms (chronic intermittent peritoneal dialysis [CIPD], chronic ambulatory peritoneal dialysis [CAPD], and chronic cyclic peritoneal dialysis [CCPD]) is an accepted method of renal replacement therapy,[1,2] we have reserved its use in our unit to patients with diseases that could complicate their course on hemodialysis.[3,4] We describe 28 such cases of patients on CIPD using automatic cycler machines.

Patients

Twenty-eight patients (16 females, 12 males)

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were studied. Age distribution was 6 to 74 years. Duration of dialysis treatment at the time of data analysis was 4 to 60 months.

The various causes of the renal disease are shown in Table 1. Forty-three percent of the patients presented with end-stage renal disease and bilaterally small kidneys, and therefore undetermined etiology. Diabetic nephropathy was the cause in 18%, glomerulonephritis in 14%, and hypertensive nephrosclerosis in 11%. Renal calculi was the cause in two patients and there were single cases of lupus nephritis and tubulointerstitial disease (pyelonephritis).

The indications for peritoneal dialysis were: severe cardiovascular disease (ischemic heart disease), cerebrovascular disease (cerebral hemorrhage, infarction), vascular access failure, retinal hemorrhage, a 6-year-old child, a patient who refused hemodialysis, and one patient who was transferred to our unit already on peritoneal dialysis (Table 2).

TABLE 1. *Etiology of renal disease.*

Cause	No.	Percentage
ESRD (unknown)	12	43
Diabetes	5	18
Glomerulonephritis	4	14
Hypertension	3	11
Renal calculi	2	7
SLE	1	3.5
Tubulointerstitial (pyelonephritis)	1	3.5
Total	28	

ESRD = end-stage renal disease, SLE = systemic lupus erythematosus.

TABLE 2. *Indications for chronic intermittent peritoneal dialysis.*

Indication	No.	Percentage
Cardiovascular disease	8	28.5
Cerebrovascular accident	8	28.5
Vascular access failure	8	28.5
Young age (6 years old)	1	3.5
Refused hemodialysis	1	3.5
Retinal hemorrhage	1	3.5
Transfer from other hospital	1	3.5
Total	28	

Method

A double-cuff Tenckhoff catheter is placed with the patient under local anesthesia while in the operating room. On the patient's arrival at the ward, continuous manual peritoneal dialysis is started, initially using 1000-ml exchanges of isotonic 1.5% dialysate with no dwell time for the first ten exchanges. Dwell time is then increased to 10 minutes if no leakage is seen.

After the initial 48 hours, dialysis is performed on alternate days for the first week. During that period the dwell time is increased to 15 minutes and the volume of exchanges gradually increased to 2000 ml.

The patient is then placed on maintenance peritoneal dialysis carried out three times per week using an automatic cycler machine (AMP 80/2). The machine is set to operate each cycle over 50 minutes (25 minutes inflow and dwell and 25 minutes drain). Each treatment consists of 18 to 20 cycles with each exchange consisting of 2000 ml of dialysate, giving the patient about 45 to 50 hours of peritoneal dialysis per week.

The dialysate comes in a two-liter soft plastic bottle containing sterile nonpyrogenic formulation and consisting of (in milliequivalents per liter) sodium, 132; chloride, 102; calcium, 3.5; magnesium, 1.5; and lactate, 35. Isotonic (1.5% dextrose) or hypertonic (4.25% dextrose) solutions are used according to the ultrafiltration need.

Potassium chloride is added to the dialysate according to the potassium status of the patient. Heparin (250 units per liter of dialysate) is added only during episodes of peritonitis or when excess fibrin strands are seen in the drainage fluid.[5] In diabetic patients, regular insulin is added to the dialysate (5 units per liter of isotonic and 15 units per liter of hypertonic), but the last two cycles are insulin free.

During routine dialysis, 8 two-liter bottles are hung up simultaneously (only one bottle contains the additives) and are all connected by means of an eight-pronged tubing set to the chamber of the machine that houses the "tube occluding organizer," after which dialysate passes via one tube to a heater and then to the patient. At the end of each treatment, 300 ml of isotonic dialysate is infused and left in the peritoneal cavity.

Results

Figure 1 shows the improvement in blood urea nitrogen, creatinine, and acid-base status averaged for all patients. There were 11 episodes of failure to drain in ten patients. Tunnel infections occurred in one patient. These complications were managed by replacement of the catheter. There were two instances of leakage around the catheter exit site and this was managed by suturing. There were 14 skin exit site infections that occurred in eight patients (eight *Pseudomonas*, five *Staphylococcus aureus*, and one coliform). Local antiseptics and combined systemic and intraperitoneal antibiotics resulted in eradication of the infection in all but two patients who had protrusion of the Dacron cuff, which necessitated replacement of the catheter.

Peritonitis was defined by the occurrence of two of the following criteria in any combination: the presence of organisms on gram-stained specimens of peritoneal dialysis fluid or in culture of the fluid; cloudy fluid with inflammatory cells (white blood cells); and symptoms and signs of peritoneal inflammation. There were 16 episodes of culture-positive peritonitis in ten patients (nine *Pseudomonas*, six *S. aureus*, one diphtheroid), giving an incidence of 0.48 episodes per patient year.

Eosinophilic peritonitis[6] (defined as cloudy fluid with no symptoms of peritoneal inflammation and no organisms isolated, but eosinophils in the peritoneal fluid) occurred eight times in three patients.

Sclerosing peritonitis (ultrafiltration failure) occurred in one patient who has been on dialysis for 60 months and who suffered several episodes of peritonitis.

Our protocol for treating peritonitis involves conversion to manual dialysis with no dwell time until the fluid becomes clear and addition of heparin to dialysate during the peritonitis episode. Antibiotic treatment is started using gentamicin (5 mg/L) and cefazolin (100 mg/L) administered intraperitoneally, in addition to a single loading systemic dose, until sensitivity results determine the appropriate antibiotic (administered intraperitoneally). Antibiotics are usually continued until the peritonitis subsides and three negative cultures are obtained. The catheter was changed in three of the patients with peritonitis, in two patients because of inability to drain and in one because of persistent exit site skin infection with protrusion of the Dacron cuff.

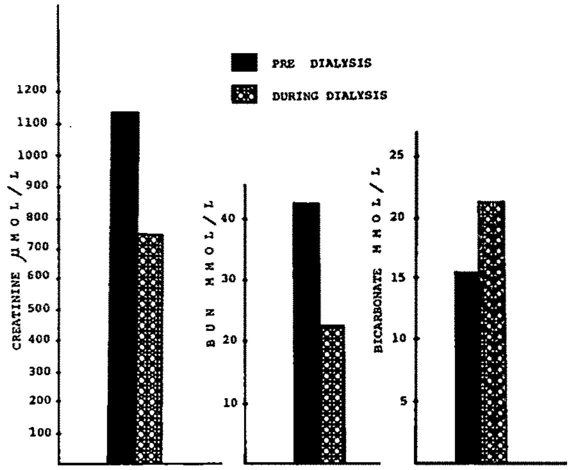

FIGURE 1. Levels of blood urea nitrogen, creatinine, and bicarbonate before and during chronic intermittent peritoneal dialysis.

Other problems encountered include pericarditis in two patients and hepatitis B surface antigen positivity in three patients (two with elevated liver enzymes). Hemorrhagic dialysate drainage occurred in one female patient and resolved spontaneously. Increased cholesterol content above 6.4 mmol/L occurred in six patients and increased triglyceride content above 2.27 mmol/L in ten patients. Serum albumin concentration ranged between 33 and 38 g/L. Radiologically detected bone disease was reported in ten patients (five secondary hyperparathyroidism, one osteosclerosis, and four osteopenia).

Five patients had renal transplantations and seven are still on dialysis. Two patients were transferred to hemodialysis at their own request and three patients were transferred to other hospitals. Two patients went on to experience improved renal functions. Nine patients died, the causes of death were: pericardial effusion and tamponade, 1; ischemic heart disease and diabetes mellitus, 2; septicemia and pericarditis, 1; septicemia and diabetes mellitus, 1; intracerebral hemorrhage, 2; cerebral infarction, 1; and liver failure, 1.

Discussion

The early 1970s saw an increased interest in

CIPD for certain groups of patients with end-stage renal disease. However, to be effective, the patients should be dialyzed for between 40 and 50 hours a week. By 1978, clinical experience with CAPD was emerging.[7] This method involves four exchanges of two liters each per day with the long-dwell time at night. Solute clearance was better, and because it uses continuous equilibration dialysis, it was the most physiological method. CCPD was developed in 1980[8] as an alternative to CAPD for patients who were unwilling to interrupt their daily routine for dialysate exchange. It involves administering three cycles at night, each lasting three hours using an automatic cycler machine, with the morning cycle dwelling intraperitoneally for the next 15 hours.

Although CIPD is less efficient than CAPD and CCPD,[9] it does not require the patient and family training and correct home environment essential for a successful CAPD or CCPD program.[10] Other major advantages of CIPD are extreme simplicity, reduced incidence of pyogenic peritonitis,[11] reduced incidence of abdominal hernias, and on nondialysis days, total freedom from dialysis. The automatic cycler machines also allow one nurse to look after several dialysis patients simultaneously.

Hemodialysis units in Saudi Arabia are approaching maximum usage, and some patients with severe cardiovascular disease have a very complicated course. Such patients could benefit from peritoneal dialysis. If CAPD/CCPD is not feasible, then CIPD, as described, can be easily adopted in any nephrology unit. The complications are usually manageable and the results, even with a high-risk group such as the one described, are acceptable.

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SPECTRUM OF RENAL DISEASE IN SAUDI ARABIA

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روجعت سلسلة من ثلاثمائة وثمانين خزعة كلوية أجريت في عدة مستشفيات بالمملكة العربية السعودية وصنفت على النحو التالي: داء الكبيبات الأولي: ٢٧٥، تأثر كلوي ضمن مرض جهازي: ٧٧، وحالات متنوعة: ٢٨. أظهر التصنيف الأوسع لخزعات مرضى داء الكبيبات الأولي (٢٧٥) ١٦ حالة تغير أصغري (٨,٥٪)، ٨٠ حالة التهاب كلوي بتكاثر مسراق الكبيبة (٩,٢٩٪)، ٩٦ حالة تصلب كبيبي كلوي قطعي بؤري (٩,٣٤٪)، ٢٩ حالة التهاب كبيبي كلوي للمسراق والشعريات (٥,١٠٪)، ١٨ حالة التهاب كبيبي كلوي غشائي (٥,٦٪)، ١٦ حالة اعتلال كلوي بالغلوبلين المناعي أ (٨,٥٪)، ١٢ حالة التهاب كبيبي كلوي مترق سريع (٤,٤٪) و٨ حالات التهاب كبيبي كلوي تال لالتهاب جرثومي (٩,٢٪). أفضت مقارنة نتائجنا بنتائج دراسات نشرت سابقا إلى أن تواتر تصلب كبيبات الكلى القطعي البؤري في سلسلتنا أعلى من مثيله في معظم السلاسل المعروفة عن البلدان الأخرى، بينما يعتبر معدل انتشار الاعتلال الكلوي بالغلوبلين المناعي أ منخفضا نسبيا. كما كان الغياب التام للالتهاب الكبيبي الكلوي للمسراق والشعريات من النوع الثاني (داء الرواسب الكثيفة) من الفروق الهامة أيضا. تظهر هنا الحاجة إلى مزيد من الدراسات لتأكيد هذه النتائج وتحديد العوامل المسؤولة عن هذه الفروق.

A series of 380 kidney biopsies performed at several institutions in Saudi Arabia was reviewed and categorized as follows: primary glomerular disease, 275; renal involvement in systemic disease, 77; and miscellaneous, 28. The 275 biopsy specimens from patients with primary glomerular disease were further classified and revealed minimal-change disease in 16 (5.8%), mesangial proliferative glomerulonephritis in 80 (29.09%), focal segmental glomerulosclerosis in 96 (34.9%), mesangiocapillary glomerulonephritis in 29 (10.5%), membranous glomerulonephritis in 18 (6.5%), IgA nephropathy in 16 (5.8%), rapidly progressive glomerulonephritis in 12 (4.4%), and postinfectious glomerulonephritis in 8 (2.9%). Comparison of our findings with those from previously published studies indicated that the frequency of focal segmental glomerulosclerosis in our series is higher than that for most series reported for other countries, while the incidence of IgA nephropathy is relatively low. Another significant difference was a complete absence of mesangiocapillary glomerulonephritis type II (dense-deposit disease). Additional studies are needed to further confirm these findings and identify the factors responsible for the differences.

Renal disease is an important cause of morbidity and mortality in the Saudi population. However, there have been only a few studies dealing with the prevalence of various types of renal diseases in the country.[1-4] In a study based on 147 renal biopsies and published from our institution, a relatively high proportion of focal segmental glomerulosclerosis (FSGS) and a low frequency of membranous glomerulonephritis (MGN) and amyloidosis were noted.[3] A subsequent study from another hospital in Riyadh revealed a relatively high frequency of mesangial proliferative glomerulonephritis (MPGN).[4]

At King Faisal Specialist Hospital and Research Centre, we have had the opportunity to study

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large numbers of kidney biopsy specimens obtained at our hospital and several other institutions from within the Kingdom. These specimens were reviewed in order to establish the spectrum of renal disease in Saudi Arabia. It is hoped that, since the specimens in our series come from several institutions, our findings will reflect more accurately the relative proportion of various renal diseases in the country.

Material and Methods

A total of 544 renal biopsy specimens examined in our laboratories between July 1983 and August 1988 were reviewed. Of them, 57 were excluded because of insufficient amount of tissue (27), end-stage renal diseases (14), nonspecific changes (11), or no significant abnormalities (5). Another 107 biopsies obtained from transplanted kidneys were also excluded. The remaining 380 biopsies form the subject of this report. Two hundred fourteen biopsies were done at King Faisal Specialist Hospital and the remaining 166 biopsy specimens were obtained from several hospitals throughout Riyadh and other parts of the Kingdom. More than one specimen from the same patient was counted as one.

Attempt was made to study all tissue by light microscopy as well as immunofluorescent and electron microscopy, but in some cases either immunofluorescent or electron microscopy could not be performed because of insufficient tissue. Specimens received from institutions outside Riyadh were studied only by light and electron microscopy. Thus, 310 biopsies were examined by electron microscopy and 356 by immunofluorescent microscopy.

Patient age varied from 3 months to 76 years; 156 patients were 16 years or younger, and 224 were older than 16. There were 203 males and 177 females. The ethnic mix was as follows: 304 patients (80%) were Saudi, 65 (17%) were expatriates, and 11 (3%) patients were of unknown nationality.

Results

The 380 biopsies were classified into three groups: primary glomerular disease, 275 (72.4%); renal involvement in systemic diseases, 77 (20.2%); and miscellaneous, 28 (7.4%). The 275 biopsies showing primary glomerular disease were further divided into several groups, according to diagnosis, and these were additionally divided into adult and pediatric patient groups (Table 1).

Minimal-Change Disease, Mesangial Proliferative Glomerulonephritis, and Focal Segmental Glomerulosclerosis

Of the 275 biopsies with primary glomerular disease, 96 (34.9%) showed FSGS, 80 (29.1%) showed MPGN, and 16 (5.8%) showed minimal-change disease (MCD). Patients in the pediatric age group showed the following proportions: FSGS (40.1%), MPGN (29.9%), and MCD (11%). Figures 1 to 3 show typical microscopic findings for these three diseases.

Mesangiocapillary (Membranoproliferative) Glomerulonephritis

Twenty-nine biopsies revealed mesangiocapillary glomerulonephritis (MCGN), representing 10.5% of the cases of primary glomerular disease. Patient age in this group ranged from 7 to 54 years and there were 17 males and 12 females (male to female ratio, 1.5:1). Twenty-seven (93%) of the patients had type I MCGN, and two (7%) had type III. None of the biopsies revealed type II MCGN (dense-deposit disease).

TABLE 1. *Relative incidence of various lesions in patients with primary glomerular disease.*

Type of lesion	All patients no. (%)	Adults no. (%)	Children no. (%)
MCD	16(5.8)	2(1.3)	14(11.0)
MPGN	80(29.1)	42(28.3)	38(29.9)
FSGS	96(34.9)	45(30.4)	51(40.1)
MCGN	29(10.5)	22(14.8)	7(5.5)
MGN	18(6.5)	16(10.8)	2(1.5)
IgAN	16(5.8)	9(6.0)	7(5.5)
RPGN	12(4.4)	9(6.0)	3(2.3)
PIGN	8(2.9)	3(2.0)	5(3.9)
Total	275	148	127

MCD = minimal-change disease; MPGN = mesangial proliferative glomerulonephritis; FSGS = focal segmental glomerulosclerosis; MCGN = mesangiocapillary (membranoproliferative) glomerulonephritis; MGN = membranous glomerulonephritis; IgAN = IgA nephropathy; RPGN = rapidly progressive (crescentic) glomerulonephritis; PIGN = postinfectious glomerulonephritis.

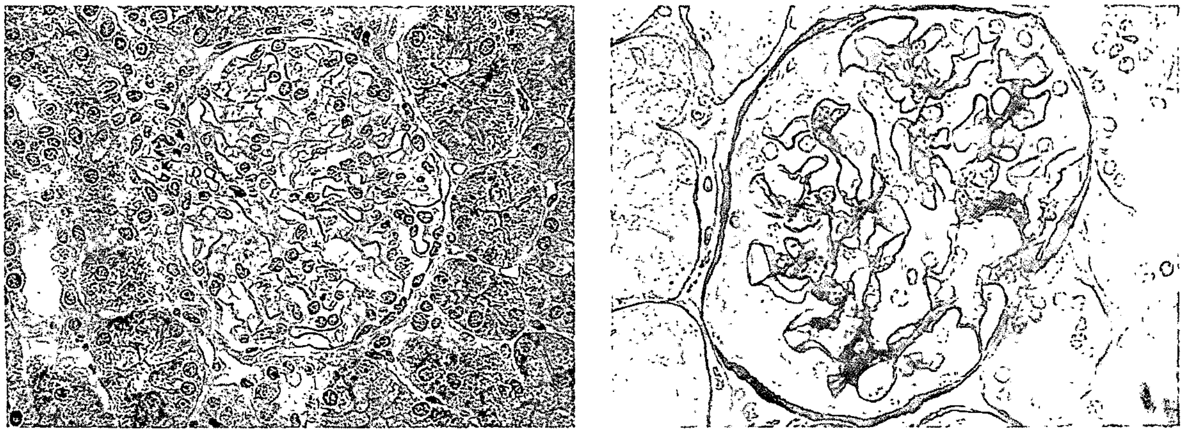

FIGURE 1. (Left) A glomerulus showing features of minimal-change disease. The capillaries and mesangium are within normal limits. (Hematoxylin-eosin; original magnification, × 250.) (Right) A glomerulus from minimal-change disease featuring essentially normal mesangial areas and capillary basement membranes. (Jones Stain; original magnification, × 250.)

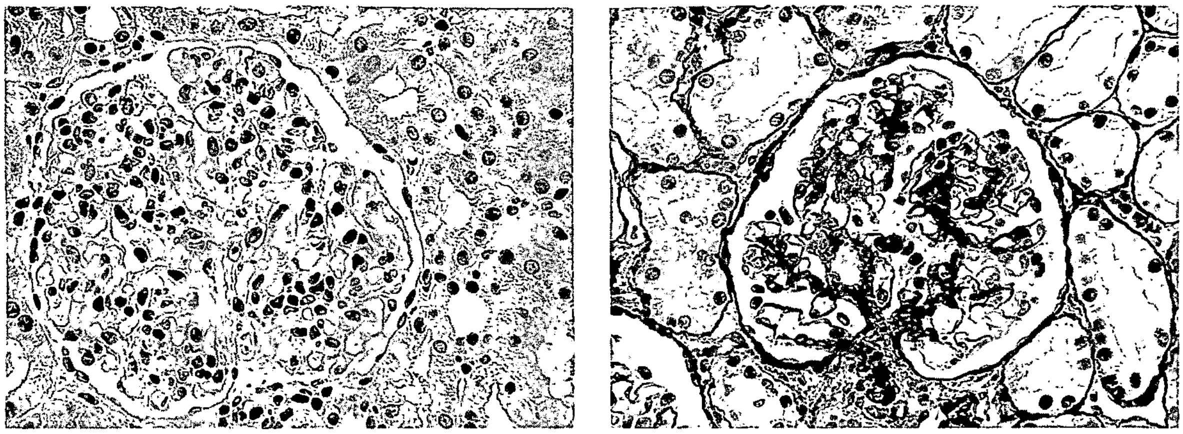

FIGURE 2. (Left) A representative glomerulus from mesangial proliferative glomerulonephritis. There is mild diffuse mesangial prominence. (Hematoxylin-eosin; original magnification, × 250.) (Right) Diffuse mesangial prominence in mesangial proliferative glomerulonephritis. (Jones stain; original magnification, × 250.)

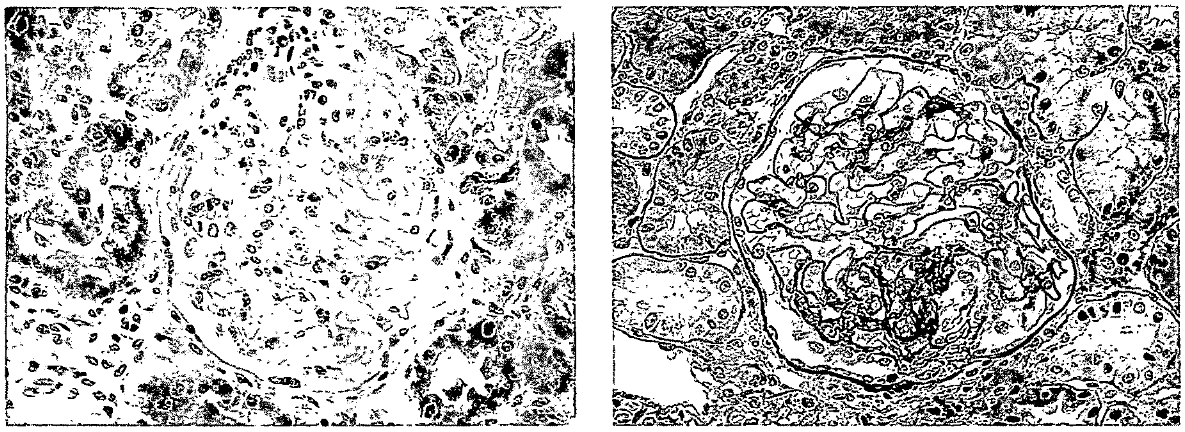

FIGURE 3. (Left) Glomerulus with a typical area of segmental sclerosis in a renal biopsy with focal and segmental glomerulosclerosis. (Hematoxylin-eosin; original magnification, × 250.) (Right) Glomerulus with focal and segmental glomerulosclerosis, but only part of the glomerulus is involved by sclerosis. (Jones stain; original magnification, × 250.)

Rapidly Progressive (Crescentic) Glomerulonephritis

Rapidly progressive glomerulonephritis (RPGN) was seen in 12 of the biopsies, constituting 4.4% of the cases of primary glomerular disease. Patient age ranged from 8 to 50 years and there were seven male and five female patients. An underlying pathogenic mechanism was immune complex disease in nine and anti-glomerular basement membrane (GBM) disease in one. No underlying immunological process could be found in the remaining three patients.

Membranous Glomerulonephritis

MGN was seen in 18 (6.5%) of the biopsies from patients with primary glomerular disease. Patient age ranged from 7 to 54 years and there were seven male and 11 female patients (male to female ratio, 1:1.5).

IgA Nephropathy

IgA nephropathy (IgAN) was diagnosed in 16 specimens, representing 5.8% of the cases of primary glomerular disease. The age range in this group of patients was 3 to 48 years. There were 11 male and five female patients (male to female ratio, 2:1). Two of the patients belonged to a single family, suggesting the possibility of familial IgAN.

Postinfectious Glomerulonephritis

A diagnosis of postinfectious glomerulonephritis (PIGN) was rendered in eight (2.9%) of the specimens from patients with primary glomerular disease. The age of these patients ranged from 6 to 29 years; six were male and two were female (male to female ratio, 3:1).

Renal Involvement in Systemic Disease

Lupus nephritis was diagnosed in 36 of the biopsies. The age range for this group of patients was 12 to 53 years and seven were male and 29 were female (male to female ratio, 1:4). Using WHO classification, the glomerular lesions were classified as follows: Class I (1), Class II (3), Class III (5), Class IV (16), Class V (6), Class III and V (4), and Class IV and V (1). Renal involvement in association with several other systemic diseases was noted in an additional 41 biopsies. Details of these cases are given in Table 2.

Miscellaneous Group

There were 28 biopsies in this group. The various diagnoses in these biopsies are given in Table 3.

Comparison with Biopsy Series from Other Countries

The results from our study were compared with those from a number of studies published from different parts of the world. Valid comparison, however, was not always possible because the study designs varied concerning both the criteria for patient selection as well as the extent of the pathological investigations. This could affect the pathological characterization. Other problems encountered include: some studies excluded

TABLE 2. *Renal involvement in systemic disease.*

Disease	No.
Lupus nephritis	36
Hemolytic uremic syndrome	8
Henoch-Schonlein purpura	7
Severe hypertension	7
Amyloidosis	4
Diabetes	4
Vasculitis	3
Sjogren's disease	1
Behcet's disease	1
Sarcoidosis	1
Subacute bacterial endocarditis	1
Scleroderma	1
Sickle cell disease	1
Glycogen storage disease	1
Total	77

TABLE 3. *Details of miscellaneous diagnosis in 28 biopsies.*

Diagnosis	No.
Unexplained immune complex glomerulonephritis	4
Benign familial hematuria	5
Acute tubular necrosis	5
Interstitial nephritis	4
Pre-eclampsia	2
Post-partum renal failure	3
Oxalosis	1
Infantile polycystic disease	1
Fanconi's syndrome	1
Alport's syndrome	2
Total	28

adults and others children; some studies only included patients with nephrotic syndrome whereas others included all patients with glomerular disease. In some series, all patients with nephrotic syndrome underwent biopsy, while in others only patients with steroid-resistant or frequently relapsing nephrotic syndrome had biopsy specimens taken. Electron microscopy and immunofluorescent studies were also not consistently done in all studies.

Tables 4 and 5 show data from these studies that have been recalculated to indicate the relative frequencies of the various lesions in a comparable manner. The category of primary glomerular nephritis is heterogeneous and includes IgAN and mesangial proliferative, diffuse endocapillary, focal proliferative, and crescentic glomerulonephritis. It would be more appropriate to subdivide this category but the information from the other published studies is not adequate enough to allow this.

Discussion

The most frequently diagnosed lesion in patients with primary glomerular disease was

TABLE 4. *Relative frequency of various types of glomerular lesions among adults in different countries.*

Country	No. of patients	MCD	FSGS	PGN*	MCGN	MGN
South Africa (black)[16]	252	27(10.7%)	9(3.5%)	72(28.5%)	90(35.7%)	54(21.4%)
South Africa (Indian)[16]	75	16(21.3%)	3(4.0%)	30(40.0%)	10(13.3%)	16(21.3%)
Tunisia[27]	304	49(16%)	49(16%)	91(30%)	51(16.9%)	64(21%)
Sudan[28]	40	7(17%)	5(12%)	15(38%)	–	13(33%)
Singapore[29]	607	190(31.3%)	66(10.9%)	316(52%)	14(2.3%)	21(3.5%)
Hong Kong[5]	271	75(27.7%)	64(23.6%)	59(21.8%)	29(10.7%)	44(16.2%)
Malaysia[30]	866	427(49.3%)	54(6.2%)	306(35.3%)	24(2.71%)	55(6.3%)
United Kingdom[31]	272	83(30.5%)	30(11.0%)	43(15.8%)	47(17.2%)	69(25.3%)
India[32]	98	28(29%)	–	38(39%)	16(16%)	16(16%)
Ghana[7]	31	3(10%)	11(36%)	8(25%)	4(13%)	5(16%)
Saudi Arabia (present study)	148	2(1.3%)	45(30.4%)	63(42.5%)	22(14.8%)	16(10.8%)

*PGN includes IgA nephropathy, diffuse endocapillary proliferative glomerulonephritis, focal proliferative glomerulonephritis, crescentic glomerulonephritis, and mesangial proliferative glomerulonephritis.

PGN = primary glomerulonephritis; MCD = minimal-change disease; FSGS = focal segmental glomerulosclerosis; MCGN = mesangiocapillary (membranoproliferative) glomerulonephritis; MGN = membranous glomerulonephritis.

TABLE 5. *Relative frequency of various types of glomerular lesions among pediatric patients in different countries.*

Country	No. of patients	MCD	FSGS	PGN*	MCGN	MGN
South Africa (black)[33]	67	10(14.9%)	4(5.9%)	20(29.8%)	6(8.9%)	27(40.2%)
South Africa (Indian)[33]	53	42(79.2%)	2(3.7%)	5(9.4%)	2(3.7%)	2(3.7%)
Kenya[34]	48	10(20.8%)	5(10.4%)	23(48%)	5(10.4%)	5(10.4%)
India[35]	187	150(80%)	11(5.8%)	19(10.1%)	4(2.1%)	3(1.6%)
Iran[6]	310	71(22.9%)	98(31.6%)	78(25.1%)	47(15.2%)	16(5.2%)
International study[36]	521	398(76.4%)	45(8.6%)	31(6.0%)	39(7.5%)	8(1.5%)
Hong Kong[5]	114	52(45.6%)	10(8.7%)	30(26.3%)	2(1.7%)	20(17.7%)
France[37]	387	209(54.0%)	47(12.1%)	41(10.5%)	53(13.6%)	37(9.5%)
Saudi Arabia (present study)	127	14(11.0%)	51(40.1%)	53(41.7%)	7(5.5%)	2(1.5%)

*PGN includes IgA nephropathy, diffuse endocapillary proliferative glomerulonephritis, focal proliferative glomerulonephritis, crescentic glomerulonephritis, and mesangial proliferative glomerulonephritis.

MCD = minimal-change disease; FSGS = focal segmental glomerulosclerosis; PGN = primary glomerulonephritis; MCGN = mesangiocapillary (membranoproliferative) glomerulonephritis; MGN = membranous glomerulonephritis.

FSGS and this represented 34.9% of the cases. Among the adult and pediatric patients, it constituted 30.4% and 40.1% of the cases, respectively. In most countries the frequency of FSGS is less than 15% (Tables 4, 5). However, a higher incidence of FSGS has been reported from Hong Kong[5] (23.6% adults), Iran[6] (31.6% pediatric), and Ghana[7] (36% adult). Thus it appears that the frequency of FSGS in Saudi Arabia is higher than that elsewhere in the world. The reasons for this, however, are not understood. Since King Faisal Specialist Hospital and Research Centre, where most of the biopsy specimens originated, is a tertiary care hospital, it tends to receive more patients with steroid-resistant nephrotic syndrome and this could account for the high frequency of FSGS. However, since the relative proportion of other causes of steroid-resistant nephrotic syndrome such as MGN and MCGN is not increased in our series, we believe that the patient selection inherent in the pattern of referral is probably not a significant factor. Furthermore, since many of the published series also originated from tertiary care institutions, patient selection may not alone account for the high frequency of FSGS in our patients. Additional epidemiological studies are needed to understand the various factors responsible for the high frequency of FSGS in Saudi Arabia.

The second most common diagnosis in our series was MPGN. This lesion is characterized histologically by the presence of mild to moderate mesangial hypercellularity with varying degrees of expansion of the mesangial matrix.[8-12] Immunofluorescent microscopy usually will reveal mesangial IgM deposition. Clinically this disease is closely related to other causes of idiopathic nephrotic syndrome, such as MCD and FSGS. There is considerable controversy in the literature regarding the significance of mesangial proliferation and/or mesangial IgM deposition. Some believe that these features have no prognostic significance and regard them as part of the spectrum of MCD; others argue that the changes indicate a poorer prognosis and should therefore be distinguished from MCD.[8-12] In some series, mesangial prominence and IgM deposition have been categorized separately as diffuse mesangial proliferation and IgM nephropathy.[8,9] In view of this lack of uniformity regarding the reporting of MPGN, a meaningful comparison of its relative frequency with that from other series is not possible.

The diagnosis of IgAN was made in 16 (5.8%) of the cases of primary glomerular disease. This figure varies considerably from one country to another. These countries can be categorized into three groups according to the relative incidence of IgAN: Group 1 (less than 15%): U.S.A., Canada, U.K., Mexico, Chile, Brazil, Tunisia, Thailand, Switzerland, Portugal, India, New Zealand, Hungary; Group 2 (15-30%): France, Scandinavia, West Germany, Bulgaria, Italy, Spain, Malaysia, Australia, Israel, Netherlands; Group 3 (more than 30%): Japan, China, Taiwan, Hong Kong, Singapore, Korea.[13] From our data, it appears that Saudi Arabia belongs to the first group with a relatively low incidence of IgAN, but the frequency may also vary considerably among the various population groups within the same country. For example, the incidence of IgAN among American blacks is significantly lower than that found in American whites.[14] In New Mexico (U.S.A.), the American Indian population seems to have a higher incidence of IgAN compared to Anglo and Hispanic populations.[15] In South Africa, IgAN among blacks is considerably less frequent than in the Indian population.[16] To the best of our knowledge, no specific region or ethnic group with a relatively high incidence of IgAN has been identified in Saudi Arabia.

RPGN was diagnosed in 12 (4.4%) of the cases of primary glomerular disease. This is well within the 3 to 7% incidence cited in several published reports.[17] Three groups of patients with RPGN are currently recognized: approximately 20% have anti-GBM nephritis, 40% have an immune complex-mediated glomerulonephritis, and 40% have RPGN without immune deposits.[17] In our study, 9 out of 812 (75%) of the biopsy specimens revealed immune complex-mediated disease, one (8%) showed anti-GBM disease, and two (17%) had no immune deposits. Thus, there appears to be a preponderance of immune complex-induced RPGN in our series; however, since the number of cases is relatively small, no firm conclusions can be drawn.

MCGN was diagnosed in 19 (10.5%) of the cases of primary glomerular disease. This is similar to the percentages reported from several other studies. Of these, 27 (93%) were classified as type

I (with subendothelial deposits) while the remaining two (7%) showed features of type III MCGN (with intramembranous and subepithelial deposits). None of the specimens showed type II MCGN (dense-deposit disease). The reported frequency of type II MCGN varies from 15 to 48%.[18] Series originating from Western countries cited 450 cases of MCGN, of which 342 (76%) were type I or type III and 108 (24%) were type II.[19-22] In light of this, the absence of type II MCGN in our series seems very relevant.

In our series, 36 specimens were from patients with systemic lupus erythematosus. The renal lesions were categorized according to WHO classification.[23] The relative frequencies of the different histological classes were similar to those reported in previously published studies. Diffuse proliferative lesions (Class IV) were the most frequent and accounted for approximately half of all cases.[24,25] Membranous nephropathy (Class V) was noted in six (16%) of the biopsies. In addition, five biopsy specimens (13.8%) revealed mixed membranous and proliferative lesions. Thus, membranous changes were present in 11 (30%) of the 36 biopsies, and this is somewhat higher than the 6 to 24% reported elsewhere for membranous nephropathy in lupus nephritis.

Within the group of systemic diseases (other than lupus) involving the kidney, hemolytic uremic syndrome, Henoch-Schonlein purpura, and malignant hypertension were the most common (Table 3). Amyloidosis was noted in four cases, which represents 1.1% of all the native kidney biopsy specimens. A similarly low incidence of amyloidosis was reported in a review of renal biopsies from our institution.[3] The incidence of amyloidosis in biopsy series varies considerably among various countries in the Middle East and other regions of the world. In Jordan, Lebanon, Israel, Turkey, Tunisia, and Abu Dhabi, there is a relatively high frequency of amyloidosis, varying from 11.1 to 32.4% of all the renal biopsies.[3] This is most probably related to the prevalence of familial Mediterranean fever in these countries.[26] In other countries such as India, Germany, Sweden, and U.S.A., the incidence is much lower, varying from 1.25 to 3.3% of the biopsies.[3]

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MALE INFERTILITY: 155 CONSECUTIVE CASES

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تراجع هذه الورقة أول مائة وخمس وخمسين حالة عقم لدى الرجال شوهدت في المستشفى العسكري بالرياض خلال السنوات الثلاث ١٩٨١ - ١٩٨٣م. كان معدل انتشار قصور الخصية الأولي مجهول السبب مرتفعا (٤٦٪) وكذا قلة النطاف الغامض (٢٧٪) وفقد النطاف الانسدادي (٢٧٪). كانت شواذ المني أكثر شدة من مثيلاتها في البلدان الغربية وينسب عدد هام من حالات العقم إلى عامل يختص بالذكور. وقد تم تأكيد العلاقة، بين غياب الإنطاف المشاهد على خزعة الخصية وارتفاع مستويات الهورمون المنبه للجريبات. كما رافقت القيلة الدوالية الصفنية تغيرات نسيجية شديدة في الخصية، ولذا فإن جراحة القيلة الدوالية لم تؤدِ إلى تحسين فرص الحمل، كما هو الحال في الغرب.

This paper reviews the first 155 cases of male infertility seen at the Riyadh Armed Forces Hospital during the three-year period, 1981 to 1983. There was a high incidence (46%) of primary testicular failure of unexplained etiology as well as idiopathic oligospermia (27%) and obstructive azoospermia (27%). Semen abnormalities were more profound than those seen in the West and a significant number of infertility cases were due to the male factor alone. The relationship between absent spermatogenesis on testicular biopsy and raised follicle stimulating hormone levels is confirmed. Scrotal varicoceles were associated with profound histologic testicular changes, and therefore varicocele surgery did not improve the chances of pregnancy, as reported in the West.

Male infertility represents a major contributor to the overall problem of infertility in Saudi Arabia.[1] One hundred fifty-five male patients between the ages of 18 and 50 years were seen between 1981 and 1983 at our urology clinic. Most of the patients were young, healthy males presenting with infertility only. We will discuss the incidence and pattern of the problem and compare our findings with those from other centers. The various findings from semen analysis, hormonal status, and testicular biopsy are presented, and their value in the management or prognosis of such cases is summarized. The management of azoospermia and the problems of oligospermia are also discussed, especially in relation to hormonal analysis and the histologic picture found on testicular biopsy. The role and results of surgical intervention in the treatment of varicocele associated with subfertility are also discussed.

Patients and Methods

The records of the first 155 consecutive patients with male infertility seen between 1981 and 1983 at the Riyadh Armed Forces Hospital were retrospectively reviewed. All investigations were carried out at the hospital.

Various known contributory causes to infertility were sought, i.e., childhood cryptoorchidism or orchidopexy, or cases with a history of mumps orchitis, diabetes, testicular torsion, viral illnesses, or sexually transmitted diseases. Cases were also screened for history of exposure to occupational chemicals,[2] drugs, and any hormonal treatment. The spouse's health was also assessed, and a full gynecology report requested if a female factor of subfertility was suspected.

Investigations included the mean findings from two of three semen analysis samples and hormonal profile (serum follicle-stimulating hor-

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mone [FSH], luteinizing hormone [LH], prolactin, and testosterone). Testicular biopsy with hematoxylin-eosin staining was performed. Scrotal exploration with vasography was performed when indicated.

Results

Of the 155 patients, 141 (90.9%) were Saudis and 14 (9%) were non-Saudis. Two hundred twenty-nine patients (83%) had primary infertility and 26 (17%) had secondary infertility. Our method of semen analysis (i.e., the mean of two of three analyses) follows that of MacLeod:[3] the ejaculate volume should be 1.5 to 5.0 ml; sperm density, greater than 20 million per milliliter; motility, greater than 60%; and morphology, greater than 60% normal. There should also be no significant pyospermia or any hyperviscosity. Comparison of semen abnormalities in our patient group with those seen at the University of Pennsylvania study[2] between 1974 and 1976 (Table 1) reveals that azoospermia and oligospermia are the most common disorders, indicating a high incidence of testicular dysfunction and disease. Sperm motility was the most common disturbance seen in an American study, and this could be related to the high incidence of varicoceles observed. Therefore, more profound semen abnormalities are seen in our patient population.

Histopathologic examination of testicular tissue included assessment of all components, including seminiferous tubules and intertubular tissues. Testicular changes were reported as: normal histology, hypospermatogenesis, maturation arrest, Sertoli-cell-only syndrome, or fibrosis and atrophy.

Seventy-one biopsies (41%) showed primary testicular failure and were associated with the diseases listed in Table 2. The morphologic pattern compared with that reported from Mount Sinai Hospital, Canada,[4] is presented in Table 3. In our Saudi population, the majority showed testicular atrophy and Sertoli-cell-only syndrome, while the Canadian population showed hypospermatogenesis of posttesticular obstruction and a minority (12%) showed Sertoli-cell-only syndrome.

The correlation between testicular histology and gonadotropin levels in our 71 patients was as follows: hypospermatogenesis, normal levels; maturation arrest, normal or elevated levels; Sertoli-cell-only syndrome, elevated FSH levels; and fibrosis and atrophy, elevated FSH and LH levels. Patients with Sertoli-cell-only syndrome and atrophy showed marked elevation of FSH, in

TABLE 1. *Distribution of semen abnormalities.*

	Present study, 155 pts, 1981-83 (%)	Univ of Pennsylvania,[2] 200 pts, 1974-76 (%)
Azoospermia	27	8
Single abnormal parameter	63	37
Motility	22.5	26
Volume	2.5	2
Morphology	11	1
Oligospermia	27	8
All parameters normal	10	55

TABLE 2. *Primary testicular failure and associated diseases in 71 patients.*

Associated diseases	No. of patients (%)
Maldescent	11(15)
Mumps orchitis	8(11)
Urinary bilharziasis	6(8)
Venereal disease	6(8)
Hepatitis-associated antigen; positive	6(8)
Varicocele	5(7)
Pulmonary tuberculosis	4(5)
Bronchitis	4(5)
Hyperprolactinemia	1(1.5)
Diabetes	1(1.5)
Lepra bacilli	1(1.5)
Sarcoid granuloma	1(1.5)

TABLE 3. *Comparative testicular biopsy results.*

Testicular biopsy result	Present study 1981–83 No. (%)	Mount-Sinai, Canada[4] 1971–79 No. (%)
Normal	–	21(29)
Hypospermatogenesis	7(10)	51(69)
Maturation arrest	11(15)	11(15)
Sertoli-cell-only syndrome	19(26)	12(17)
Fibrosis & atrophy	34(48)	–
Klinefelter's syndrome	–	3(4)
Total	71	134

keeping with failure of spermatogenesis. This is a well-recognized finding and is supported by findings from a recent study by Perry[5] from Dammam as well as by two comprehensive studies conducted in British[6] and American[7] patients. LH and testosterone levels, when found in normally androgenized males, were of little help in determining treatment or prognosis, as corroborated by the British study.[6]

With regard to semen analysis, hormonal assays, and testicular histology, our 155 patients fell into three groups: 71 patients (46%) had primary testicular failure, 42 patients (27%) had obstructive azoospermia, and 42 patients (27%) had idiopathic oligospermia. No pregnancy was achieved by the 71 patients with primary testicular failure.

The 42 patients with obstructive azoospermia, who showed no sperm in two or more ejaculates, had normal gonadotropin hormone levels and showed satisfactory spermatogenesis on testicular biopsy. Associated diseases in these patients are shown in Table 4 and the most common infertility problems in our patient population are compared with the findings in a study from Texas[7] in Table 5.

Obstruction of the ejaculatory ducts and seminal vesicle dysfunction were ruled out by the presence of fructose in the semen. Clinically diagnosed abnormalities of the epididymis and vas deferens were confirmed at transscrotal exploration and vasography. Complete vas deferens block was found in five patients (12%) and congenital absence of the vas deferens, congenital atresia of the vas deferens, and partial aplasia of the vas deferens in 1 patient each (2%).

Vasoepididymostomy was performed in 34 patients (bilateral in 23 and unilateral in 11) using the procedure of Turner.[8] Our postoperative results, as compared to those in Cleveland, Ohio,[9] and Hamburg, Germany,[10] are shown in Table 6. Five patients manifested semen improvement; two showed the appearance of sperm at three months, and this occurred at four months, six months, and 18 months after surgery in the remaining three. In one report,[9] sperm appeared as early as one month and as late as two years after operation. We considered vasoepididymostomy a failure in our patients if azoospermia persisted two years after surgery.

We regarded as idiopathic oligospermics those patients who had a sperm count below 20 million per milliliter on two or more occasions and had a normal testicular biopsy, and whose wives had no female component of infertility. The 42 patients with idiopathic oligospermia had the coexisting diseases shown in Table 7.

Recognizing the physiologic relationship of the hypothalamopituitary system to testicular function, we have used mesterolone, human chorionic gonadotropins, clomiphene citrate, and bromocriptine in an attempt to improve semen quality

TABLE 4. *Associated diseases in 42 azoospermic patients.*

Disease	No. (%)
Venereal disease	12(29)
Hepatitis-associated antigen	6(15)
Bilharziasis	5(12)
Diabetes	5(12)
Varicocele	5(12)
Orchitis	3(7)
Smallpox	3(7)
Mumps	2(5)
Pulmonary tuberculosis	1(2)

TABLE 5. *Comparison of common infertility conditions.*

	Present study (No. of patients [%])	Lipshultz[7] (No. of patients [%])
Testicular failure	66(37.93)	40(10.5)
Obstruction	37(21.2)	26(6.8)
Idiopathic oligospermia	40(22.9)	108(28.4)
Varicocele	12(6.9)	159(41.8)
Cryptoorchidism	11(6.3)	26(6.8)
Hyperprolactinemia	5(2.8)	4(1.0)
Ejaculatory failure	2(1.1)	5(1.3)
Impotence	1(0.5)	12(3.1)

TABLE 6. *Comparison of vasoepididymostomy results.*

Report	No. of patients	Semen improvement	Pregnancy
Cleveland, Ohio (Thomas[9])	25	18(72%)	–
Hamburg, Germany (Wagenknecht[10])	180 (bilateral) 55 (unilateral)	85(47%) 17(31%)	28(15%) 7(13%)
Present study	34	5(14.7)	2(6%)

and production. Comparison of our results with other centers is shown in Table 8.[11]

Mesterolone (a derivative of dihydrotestosterone that is less likely to cause testicular atrophy) was given to 15 patients until azoospermia was achieved. The drug was then stopped with the hope that spermatogenesis would start anew, with a rebound to a higher level than existed prior to treatment. Four patients showed improvement in semen quality 6 to 18 months later, but no pregnancy was achieved. This testosterone rebound phenomenon was first described by Rowley and Heller,[12] who reported a 41% pregnancy rate in 157 patients. This figure has not been equaled in other series. Therefore we are guarded in our opinion of testosterone rebound therapy, since the mechanism is only speculative. A few such patients have remained azoospermic for three years following treatment[13] and a few have achieved pregnancy but without improvement in semen.

TABLE 7. *Idiopathic oligospermia and coexisting diseases in 42 patients.*

Associated diseases	No. of patients (%)
Venereal disease	6(14)
Bilharziasis	4(9)
Hyperprolactinemia	3(7)
Bronchitis	2(5)
Varicoceles	2(5)
Mumps orchitis	2(5)
No disease	23(54)

TABLE 8. *Reported experience of treatment of idiopathic infertility.*

Agent	Report	No. of patients	Improved semen	Pregnancy
Mesterolone				
	Present study	15	4	0
	Giarola (1974)	15	0	0
	Keough (1976)	20	0	3
Human chorionic gonadotropin				
	Present study	4	2	2
	Sherins (1973)	9	0	0
	Paulson (1976)	9	4	1
Clomiphene				
	Present study	19	3	0
	Mellinga (1966)	15	11	0
	Foss et al (1973)	114	0	19
Bromocriptine				
	Present study	4	2	2

N.B. Data taken from Sherins and Howard.[11]

Human chorionic gonadotropin hormone, which increases Leydig cell activity with consequential improvement in spermatogenesis and/or motility, has been used in four of our patients (1,500 IU twice per week for 12 months). Two achieved successful pregnancies. One successful pregnancy occurred after the wife was treated for pulmonary tuberculosis. Szollosi et al[14] reviewed the cases of 160 men who all followed a similar regimen; they noted semen improvement in 34% and a 16% pregnancy rate in the wives of both hypogonadotropic and normal gonadotropic men. Thus our findings and those of others show that human chorionic gonadotropin therapy leads to improvement in the sperm count in some groups, but there is no evidence of an increased fertility rate.

Clomiphene citrate is a nonsteroidal estrogen with minimal effect that has been shown to increase pituitary gonadotropin levels, and occasionally improves semen production. It is more beneficial when given to men with low to normal FSH and LH levels in the presence of oligospermia below 20 million per milliliter.[15]

The patients in our study were given 50 mg of clomiphene once daily for three months, and this was repeated for up to nine months in 19 oligospermic men. None achieved pregnancy. Five of the patients who had normal hormone levels, satisfactory testicular biopsy, and oligospermia below 15 million per milliliter responded to the therapy in that their semen production and quality increased; in two, sperm count increased to 25 million and 41 million per milliliter. The remaining 14 patients who had normal hormone levels and hypospermatogenesis showed reduced semen quality after clomiphene treatment. Schill[16] reported a pregnancy rate of 20.7% in 367 patients treated with clomiphene. We found no evidence that clomiphene will improve the pregnancy rate though our number of patients was small and some positive responses were seen. Four of our patients had hyperprolactinemia and were given bromocriptine for three months (2.5 mg once daily). Two achieved successful pregnancies. The first patient had prolactin levels of 311 and 373 mIU/L (normal range, 70-290 mIU/L) and partial atrophy shown by testicular biopsy. After treatment, his prolactin level became normal and his wife got pregnant while he was still oligospermic with a 4.0 million per milliliter sperm count. The second patient had a prolactin level of 359 mIU/L which became normal after treatment. His semen count increased from 20 million to 111 million per milliliter. The two patients who showed no improvement remained severely oligospermic despite normal prolactin levels after treatment.

Scrotal varicocele with its well-recognized decrease in testicular function has been mentioned as the major cause of male infertility. Greenberg and Lipshultz[17] cited a rate of 30 to 50% in their study from the U.S. and Hendry et al[18] quoted a rate of 21% in their study from England. It was only 8% in our study (one of 12 patients).

In our small series of 12 patients with varicoceles, eight (66%) were oligospermics and four (33%) were azoospermics. In contrast, MacLeod[19] reported a 65% oligospermia rate and no azoospermia or testicular atrophy. However, in our varicocele study, 42% of our patients showed testicular atrophy. It is unlikely that varicocele alone is the cause of atrophy or azoospermia; more likely the varicocele coexisted with a primary testicular disease. Because of this high rate of testicular atrophy and azoospermia, we have seen poor improvement in semen quality and the pregnancy rate after varicocelectomy compared with the rates given in other studies (Table 9).

In all our patients with varicocele, both sperm counts and stress cytology have shown some improvement. Only one patient (8%) produced a successful pregnancy, and two patients (16%) showed good improvement in semen quality, which allowed the respective wives to undergo artificial insemination.

TABLE 9. *Changes in semen quality and pregnancy rate after varicocelectomy.*

Report	No. of patients	Improved semen quality (%)	Pregnancy rate (%)
Lipshultz (1982)	32	70	42
Dubin & Amelar (1975)	504	70	55
Macleod (1969)	108	70	44
Present study	12	16	8

N.B. Data taken from Greenberg and Lipshultz.[17]

Discussion

We found that infertility in a significant number of Saudis is due to the male factor alone. The more profound semen abnormalities in our patients and a high incidence (46%) of testicular atrophy and Sertoli-cell-only syndrome of unknown etiology explain our poor results from treatment.

The report from the King Faisal Specialist Hospital[20] about the deposition of IgG in the basement membrane of 13 of 30 Saudi patients, causing an antibody directed against specific antigens in the basement membrane of seminiferous tubules, in part explains the testicular damage seen in Saudi patients.

A high FSH level in our study indicates total germinal cell failure which corroborates similar findings in Britain,[6] the U.S.,[7] and Dammam.[5] Therefore testing of the FSH level has replaced testicular biopsy as a diagnostic aid for male infertility, especially in cost-conscious centers. We limit use of testicular biopsy to azoospermic patients with normal sized testes and normal hormone levels to distinguish between primary testicular failure and obstructive azoospermia. The use of testicular biopsy in cases of oligospermia is controversial, and some practitioners have found results noncontributory. We have found it useful in predicting prognosis in patients brought to us for second opinion consultation. Successful counseling of oligospermics can be given only if its etiology is better understood, including the associated phenomena of sperm autoantibodies, female cervical mucous hostility, and sperm chromosomal abnormalities, for it is well known that oligospermics have fathered children successfully.[21] The wives of our patients whose semen count increased to 4 million per milliliter motile spermatozoa were referred for artificial insemination.

The lack of good results from vasoepididymostomy (6% pregnancy rate despite positive sperm presence in epididymal smears) could be due to scar tissue formation, sperm granuloma, vas ileus, agglutinating sperm antibodies found in 60% of obstructive azoospermics,[7] and most notably poor microsurgical technique.

The incidence of varicocele in this study was small and the results suggest that varicocele is a coincidental finding rather than the cause of testicular atrophy or azoospermia. After high-ligation varicocelectomy, semen quality and production improved in 16% of patients, resulting in 8% pregnancy.

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VISCERAL LEISHMANIASIS IN THE SUDAN: CLINICAL AND HEMATOLOGICAL FEATURES

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تصف هذه المقالة السمات السريرية والدموية والاستجابة للعلاج لدى سبعة عشر (١٧) مريضا سودانيا مصابين بداء الليشمانيات الحشوي. كانت الملامح السريرية لهذه الحالات مشابهة لمثيلاتها من أثيوبيا وأفريقيا الشرقية. وكانت الحمى وتضخم الكبد والطحال وقلة الكريات البيض وقلة اللمفاويات وقلة الصفيحات من المشاهدات المألوفة. وأما التواتر المرتفع نسبيا للخلل الوظيفي الكبدي فقد كان من السمات غير المألوفة. توفي مريض واحد بالنزف المخي وآخر بالنزف الهضمي. وقد عزيت التظاهرات النزفية إلى التهاب الأوعية الناتج عن معقد مناعي وقلة الصفيحات. كانت الاستجابة لعلاج «ستيبو غلوكونات الصوديوم» جيدة.

The clinical and hematological features and response to therapy in 17 Sudanese patients with visceral leishmaniasis are described. The clinical features in our cases were similar to those described from Ethiopia and East Africa. Fever, hepatosplenomegaly, leukopenia, lymphopenia, and thrombocytopenia were common findings. An unusual feature is the relatively high frequency of hepatic dysfunction. One patient died of cerebral hemorrhage and another of gastrointestinal bleeding. Hemorrhagic manifestations were attributed to immune complex vasculitis and thrombocytopenia. The response to sodium stibogluconate was good.

Visceral leishmaniasis is endemic in several areas of the Sudan. The disease occurs in an area that extends from Kassala on the Sudanese Ethiopian border to Malakal and Nasir in the Upper Nile Province. It also occurs in the Kapoeta region of Equatoria Province in the southern Sudan and Darfur Province in the western part of the country. A form affecting children has recently been identified in Khartoum Province.[1]

The clinical features of visceral leishmaniasis have been described in patients from the provinces of the Blue Nile,[2] Equatoria,[3] Kordofan, Darfur,[4] and the Upper Nile[5] (Figure 1). Since most of the reports are at least twenty years old, we thought it worthwhile to study Sudanese visceral leishmaniasis in more depth, concentrating on aspects that were not addressed by previous investigators.

Material and Methods

Seventeen patients were seen for the first time at the Hospital for Tropical Diseases in Omdurman. The diagnosis was made by the microscopic demonstration of amastigotes in bone marrow smears and in some patients by lymph node aspiration as well.

A complete history was obtained and clinical examination performed. Investigations included: chest x-ray study, electrocardiogram, urinalysis, thick and thin blood films for malaria parasites, stool examination, peripheral blood counts, coagulation studies, and Coombs' test using monospecific anti-IgG, C3 and C4, and broad-spectrum antihuman globulin. In six patients,

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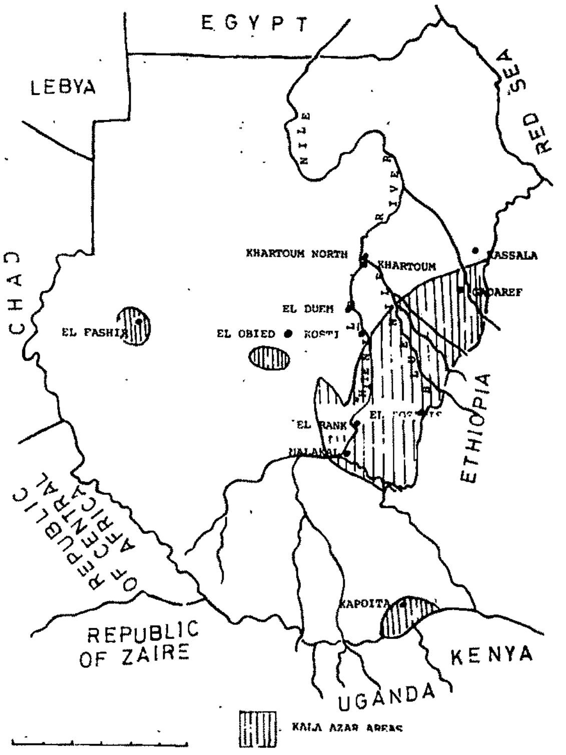

Figure 1. Map of the Sudan showing the kala-azar endemic areas.

chromium 51-labeled, heat-damaged autologous red cells were used to assess the rate of clearance and the phagocytic activity of the spleen using a liquid scintillation counter for the former and color scanner for the latter. Red cell survival and surface counting using ^{51}Cr were performed in two patients. All hematological tests were performed according to the methods of Dacie and Lewis.[6] The bone marrow examinations, blood counts, and coagulation studies were performed before treatment and two weeks after completion of the sodium stibogluconate therapy.

Immune complexes were assayed by the C1Q-enzyme linked immunosorbent assay.[7] Rheumatoid factor was tested using the Hoechest Kit (Hoechest Laboratories, West Germany).

Patients were treated with intravenous sodium stibogluconate according to the following regimen: Adults: Day 1, 2 ml IV; Day 2, 4 ml IV; Day 3 to 15, 6 ml IV. Children: the dose was calculated according to body weight as recommended by the manufacturer (Burroughs Wellcome, England).

The development of anorexia, vomiting, rashes or any new symptoms was considered evidence of toxicity. Patient progress was monitored through daily recording of morning and evening temperatures and the size of the spleen and liver.

Patients were considered cured when the bone marrow aspiration was negative for parasites, accompanied by improvement in clinical status and laboratory data.

Results

Clinical Features

All 17 patients were males and aged 10 to 48 years (mean, 24 ± 8 years). They were all farmers or laborers who came from endemic areas around Gadaref (15 patients), Darfur (one patient), and Malakal (one patient). Symptoms had lasted from 15 days to 6 months (average, 3 months). The clinical features are summarized in Table 1.

Fever, weight loss, and signs of anemia were found in all cases. Ten of the 12 patients with abdominal pain had a dull, dragging, left hypochondrial pain related to the splenic enlargement; the remaining two patients' pain was central, colicky, and associated with melena. One patient was treated in another hospital for severe diarrhea five days before he was seen by us. Six patients were jaundiced and eight had epistaxis. Two had cough that produced blood-stained sputum, clinical signs of consolidation, and multiple pulmonary opacities seen on chest radiographs. With the exception of four patients, the rest felt well, their appetite was good, and they were ambulant.

Ten patients had pitting edema of the feet. The average size of the spleen was 6.2 cm (range, 0-10.5) and the liver was 2.6 cm (range, 0-4) below

Table 1. *Frequency of symptoms and signs in 17 patients.*

Symptoms and signs	No. of patients
Fever	17
Abdominal pain	12
Pallor	17
Jaundice	6
Splenomegaly	16
Hepatomegaly	15
Rash	8
Edema	10
Epistaxis	8
Enlarged lymph nodes	10

the costal margin. Lymph node enlargement was found in ten patients. The lymph nodes were firm and discrete, and varied from 1 to 3 cm in diameter. The inguinal lymph nodes were enlarged in all the ten patients with lymphadenopathy; two patients also showed cervical and axillary lymph node enlargement. Amastigotes were demonstrated in the inguinal lymph nodes in four of the patients who had aspiration performed.

Seven patients also had schistosomiasis mansoni, and an amebic liver abscess developed in one.

Hematology

The hemoglobin concentration was low in all patients (mean, 77 ± 12 g/L). The peripheral blood films showed anisopoikilocytosis with a preponderance of macrocytes in nine patients. Slight to moderate polychromasia was common.

All patients were leukopenic, with neutropenia in 15 (88%) and lymphopenia in 16 (94%). Ten patients were still lymphopenic two weeks after sodium stibogluconate therapy, but the mean lymphocyte count rose from 0.619 ± 0.392 to 1.414 ± 0.766 × 10^9 cells per liter. Following sodium stibogluconate therapy, the seven patients with concomitant schistosomiasis developed eosinophilia. Thrombocytopenia was present in all patients. The mean platelet count was 51 ± 41 × 10^9/L. Counts below 50 × 10^9/L were found in 11 (65%) patients, and the eight patients with epistaxis also had severe thrombocytopenia.

The bleeding time was prolonged in nine patients, while the prothrombin time was only marginally prolonged in four. The partial thromboplastin time was within normal limits.

Increased cellularity of the bone marrow with hyperplasia of all elements was found in all cases. Erythropoiesis was megaloblastic in 12 patients (70%) and normoblastic in the remaining five. Variable degrees of erythrophagocytosis and leukophagocytosis by mononuclear phagocytes was a constant feature (Figure 2). No iron was seen on stained smears of bone marrow.

The half-time clearance of ^{51}Cr-labeled, heat-damaged red cells was markedly shortened in five of six patients and was prolonged in one. However, the spleen was not palpable in the latter and color scanning showed scattered activity that was most likely over the abdominal lymph nodes. Splenic scanning performed 24 hours later showed markedly increased activity, indicating sequestration and destruction of erythrocytes.

Serology

Rheumatoid factor was positive in all cases. High concentrations of immune complexes were found in five of the six cases tested (Table 2); two also had schistosomiasis.

Direct Coombs' test using monospecific anti-IgG was positive in 14 cases, and using both anti-IgG and anti-C3 was positive in three cases. Broad-spectrum anti-human globulin serum, however, yielded a negative result to the direct Coombs' test in all cases.

Response to Treatment

All patients responded well to treatment. Six-

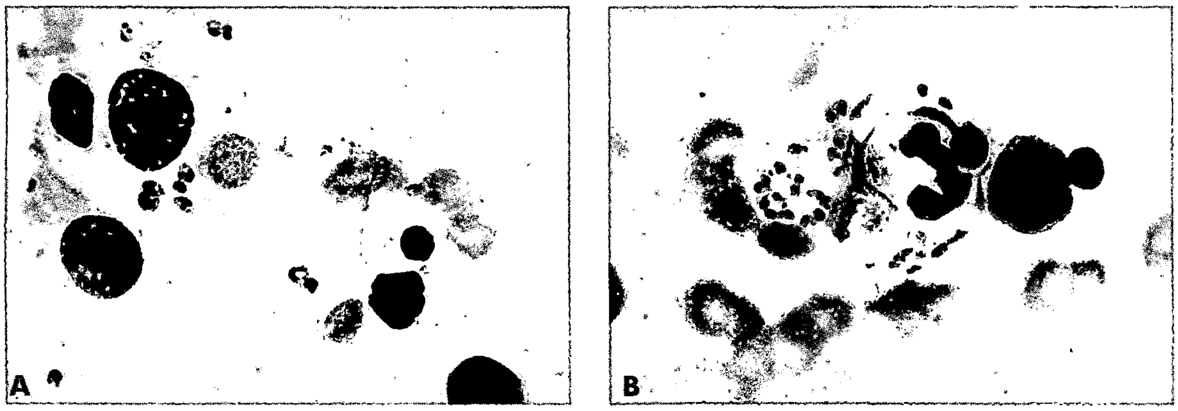

FIGURE 2. Bone marrow smear showing (A) erythrophagocytosis and (B) neutrophil phagocytosis by reticulum cells, which contain several amastigotes. (Wright stain; original magnification × 1500.)

teen eventually were discharged and were afebrile four weeks after treatment. Follow-up for longer periods was not possible. During the period of observation, the patients gained weight and felt and looked better. The spleen and liver size started to decrease, with the most dramatic reduction in large spleens. The hematological profile improved (Table 3). After the sodium stibogluconate therapy, two patients developed fever. An amebic abscess of the liver was found in one and this responded well to treatment. The other patient had a urinary tract infection that was controlled with appropriate antibiotic therapy.

One patient had had delirium for three days before the start of sodium stibogluconate therapy. Following this, he went into a coma and died. Autopsy revealed a hemorrhage in the right temporal lobe that had ruptured into the ventricular septum and subarachnoid space. This patient had the lowest platelet count in the group. He had no hypertension or vascular anomaly. A second patient died of massive intestinal hemorrhage.

Discussion

Because the cases are from a hospital population, no definite conclusions can be drawn regarding the age and sex distribution. The disease had no predilection for infants and affected more males than females,[5] but the difference in the sex distribution in our patients is attributed to the reluctance of females to seek medical care. In the outbreak which occurred in Khartoum Province, the disease was confined to children.[1] The response of visceral leishmania to treatment varies in different parts of the world.

Sodium stibogluconate was very effective in our patients, all of whom tolerated it well and have shown no relapse. A similar beneficial effect was

TABLE 2. *Immune complexes in cases of visceral leishmaniasis.*

Serum No.	Optical density	Visceral leishmaniasis	*Schistosoma mansoni* infection
1	1.24	+	+
2	0.53	+	+
3	0.32	+	−
4	1.01	+	−
5	0.82	+	−
6	0.62	+	−
7 N/2SD	0.42	−	−
8 SLE A	1.60	−	−
SLE B	1.48	−	−

N = 15 normal sera; SLE = systemic lupus erythematosus serum specimens A and B.

TABLE 3. *Hematological changes in kala-azar before and after treatment.*

	Hemoglobin (L)	PCV	MCV (fL)	MCH (pg)	MCHC (g/L)	Reticulocytes (10^9/L)	WBC (10^9/L)	Platelets (10^9/L)	Bone marrow Morphology	Bone marrow Non stain
Before treatment										
Mean ± SD	76±12	0.24±0.38	101±17.8	30 + 6.6	313 ±24	3.1 ± 0.8	2.1 ± 0.8	51 ± 41	12, megaloblastic, 5, normoblastic	Deficient in all
Range	56–106	0.16–0.33	72–130	19–34	280–350		0.85-3.885	2–13.5		
No. of cases	17	17	17	17	17		17	17		
After treatment										
Mean ± SD	89±15	0.28±0.38	90±15.4	28±5.5	307±25	3.6±2.1	30.9±1.0	163±60	8, micro-normoblastic	Deficient in all
Range	68–110	0.200-0.34	68–103	18–32	280–320	1–8	2.6–5.482	25–30	2,megaloblastic; 5, normoblastic	
No. of cases	15	15	15	15	15	15	15	15		

PCV = packed cell volume; MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; WBC = white blood cells.

observed in Indian patients who generally responded well during 10 to 20 days of treatment with antimony.[8] In East Africa the disease is more resistant to treatment, and despite the standard 30-day course of 10 mg of sodium stibogluconate per kilogram of body weight, some patients are not cured; moreover, relapse sometimes occurs after successful treatment.[9] A recent study revealed a relapse rate of 7.6% among 38 Kenyan patients who had been cured after receiving an average of 35 injections (mean dose, 405 mg/kg of antimony).[9]

Fever was a consistent finding in our patients. They had a good appetite, were usually ambulant, and felt remarkably well despite their pyrexia and emaciation. Those who suffered complications such as amebic hepatitis or urinary tract infections looked ill, lost their appetite, and were usually confined to bed. Diarrhea, which was severe in one patient, has been observed before in Sudanese kala-azar.[10]

Splenic enlargement was usual in our patients. In one patient, who had had fever for only 15 days, the spleen was not palpable. The liver was enlarged in 15 patients, but it did not exceed 4 cm in those who had schistosomiasis. Hepatic and renal dysfunctions were common in these cases, which is contrary to the findings of Kager et al in East Africa.[9] Both renal and hepatic functions improved after sodium stibogluconate therapy. The hepatic and renal manifestations and pathology in kala-azar patients will be reported (Mustafa et al and El-Hassan et al, in preparation).

All patients had anemia of varying degrees, with a multifactorial etiology. Nutritional factors have an important bearing, as patients are from a low socioeconomic group. Iron deficiency is evidenced by depletion of the bone marrow stores. The megaloblastic erythropoiesis is probably due to folate deficiency caused by poor diet as well as increased demand from greater marrow activity. A third factor in the pathogenesis of the anemia is hemolysis. There was decreased red cell survival in these patients, rapid clearance of labeled red cells from the circulation, and increased sequestration in the spleen as seen in the colored scanning. Erythrophagocytosis was seen in the bone marrow. The positive Coombs' test indicates an immune mechanism for the hemolysis. This was also suggested by others.[11,12] Musumeci et al[13] reported similar findings in Mediterranean kala-azar. The erythrocytes were positive for direct antiglobulin tests using antisera to IgG and complement C3. Erythrophagocytosis with increased deposits of hemosiderin in the liver and spleen was demonstrated in our patients. The red cells may have absorbed immune complexes on their surfaces and then been phagocytosed by cells of the reticuloendothelial system.

The leukopenia and thrombocytopenia are due to increased peripheral destruction rather than failure of production. This is shown by the increased bone marrow activity and the phagocytosis of white cells in the bone marrow. A contributory factor may be the megaloblastic hemopoietic abnormalities in some of the patients. We believe that thrombocytopenia, immune complex vasculitis, and disseminated intravascular coagulation are the major causes of the hemorrhagic manifestations.[14] The patient with the lowest platelet count died of a cerebral hemorrhage. Such hemorrhagic manifestations have been observed by others.[8,15] Decreased platelet count as well as shortened platelet survival occurred in five infants with acute kala-azar,[16] but this was not associated with hemorrhagic manifestations. Kager et al[12] have confirmed the occurrence of red cells, white cells, and platelet autoantibodies in blood specimens from their patients.[13]

The hematological parameters in our patients showed some changes even as early as two weeks after treatment. The hemoglobin concentration increased slowly even though there was no significant difference from pretreatment level. There was a consistent marked increase in platelets and white cells after therapy.

No primary skin lesions were observed in our patients. Such lesions were described by Kirk[17] from the Sudan and were seen in five of 40 patients in Kenya.[18] Post-kala-azar dermal leishmaniasis occurred in one of our patients immediately after therapy. This agrees with the observations of Kirk and Sati[2] in Sudanese kala-azar in which the eruption usually appeared during or on completion of treatment or within a comparatively short period afterward. In Indian patients, the dermatitis is reported to appear one to two years after treatment and persist for a long time.[19]

The eosinophilia that occurred following sodium stibogluconate therapy in kala-azar patients who also had schistosomiasis is difficult to explain. Eosinophils might have been destroyed, along with other formed elements of the blood, in the untreated kala-azar patients and then reappeared in the blood after therapy. Another possibility is that, during active *Leishmania* infection, there is reversible depression of T-cell function,[20] and therefore the eosinophil response to bilharzia infection, which depends on T lymphocytes, is temporarily lost.[21]

Acknowledgment

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TUBERCULOSIS OF THE STERNUM

Mahmoud Ashour, FRCS; L. Pandya, MRCP

يعتبر التدرن القصي سريريا نادر الحدوث. ونحن نشرح هنا حالتين من التدرن القصي تظاهرت إحداهما بكسور
مرضية في القص والأخرى بخراج بارد في وسط القص.

Tuberculosis of the sternum is a rare clinical entity. We describe two cases of sternal tuberculosis, one of which presented with pathologic fracture of the sternum and the other with a cold abscess in the midsternal zone.

Although tuberculosis is a common problem in Saudi Arabia, to the best of our knowledge, no cases of sternal tuberculosis have been reported. In a study of 68 patients with bone and joint tuberculosis living in Riyadh, no patient with sternal tuberculosis is described.[1]

Tuberculosis of the sternum warrants special mention because of the difficulty in diagnosis, the morbidity associated with intrathoracic spread of the disease, and the therapeutic challenge it poses. We describe two patients with sternal tuberculosis and review the literature.

Case Reports

Patient 1

A 24-year-old male university student was first seen at the Accident and Emergency Department complaining of severe chest pain following a minor blow to the chest. There was no history of tuberculosis or contact with tuberculous patients. On examination, he was in pain but not pyrexial. A soft, tender 3 × 2 cm mass was found in the midsternal region. The overlying skin was of normal color but not warm. There was no lymphadenopathy and no other swelling was found elsewhere. Respiratory and cardiovascular findings were unremarkable.

Peripheral blood examination showed hemoglobin concentration, 14.2 g/L; white cell count, 9.6×10^3 /mm^3; and erythrocyte sedimentation rate, 25 mm in the first hour; sickling test was negative. The biochemical investigations showed normal urea and electrolyte values; liver function tests, including alkaline phosphatase, protein electrophoresis, and immunoelectrophoresis, were also normal. Urine examination showed no Bence Jones protein. Tuberculin test was negative.

Posteroanterior radiograph of the chest showed no evidence of a lung lesion. Lateral radiograph of the chest showed a fracture of the midsternum surrounded by bone rarefaction (Figure 1). Computed tomography of the sternum demonstrated a destructive bone lesion involving the same area of the sternum (Figure 2). Bone scan showed increased activity with a central cold area in the middle third of the sternum (Figure 3). Galium scan also showed markedly increased activity in the same sternal zone. The rest of the skeletal survey was normal.

Malignant tumor of the sternum was suspected and operation was planned. At operation, a soft pinkish mass was found to replace a 2 × 3 cm zone of the sternum. The sternum was clearly unstable. One enlarged intercostal lymph node was found. Frozen section of the tumor tissue showed granuloma and there was no evidence of malignancy. Conservative resection of the involved zone was done and a Dacron mesh graft was used to close the sternal gap. Histologic examination of the resected specimen showed noncaseating

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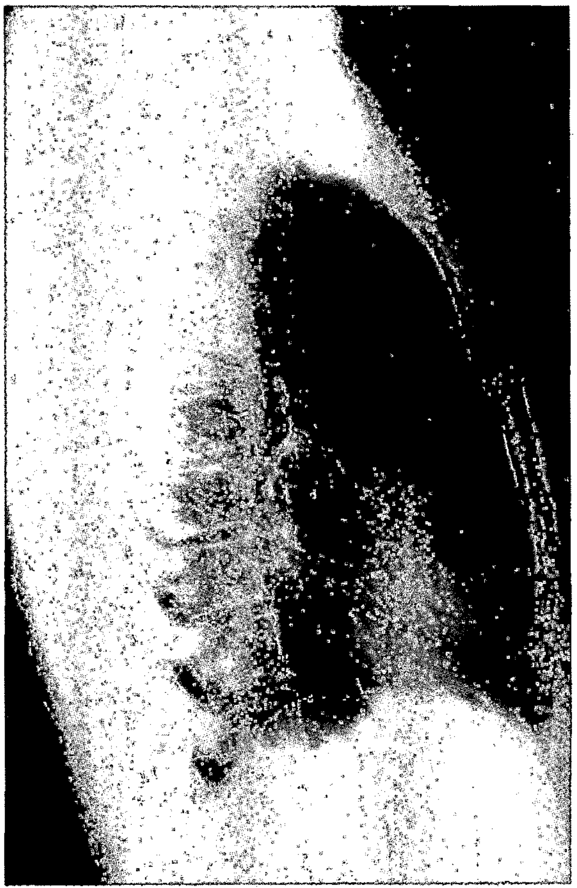

FIGURE 1. Patient 1. Lateral radiograph of the chest showing fracture of midsternum with bone rarefaction around it.

granuloma and acid-fast bacilli. Tissue culture for tuberculosis was positive. Postoperatively, the patient made an excellent recovery and he was put on the standard four antituberculous drugs. When seen a year later, he was well.

Patient 2

A 55-year-old woman was admitted with history of fever and productive cough of two months' duration. Fifteen years before she had suffered from pulmonary tuberculosis for which she received treatment. On examination, she appeared ill and pyrexial with fever of 38.5°C. A 7 × 4 cm cystic swelling was found over the midsternal zone. Examination of the respiratory system revealed poor air entry and dullness over the right lung.

Radiograph of the chest showed totally destroyed right lung, and lateral radiographs revealed bone destruction of the sternum surrounded by a large soft tissue mass. Blood examination showed hemoglobin, 99 g/L; white cell count, 10.7×10^3 /mm^3; and erythrocyte sedimentation, 130 mm in the first hour. Urea and electrolyte levels and liver function tests, including alkaline phosphatase, were normal. Urine examination showed no evidence of Bence Jones protein. Sputum was negative for acid-fast bacilli. Tuberculin test was positive; reaction radiated more than 10 mm from the injection site.

At operation, the sternum was found to be destroyed by a caseating lesion. The abscess around the sternum involved the anterior mediastinum. Histopathologic evaluation of the drained specimen showed granulomatous tissue consistent with tuberculosis. The patient was put on antituberculous treatment. Postoperatively, her condition deteriorated slowly until she died of mediastinitis and progressive bronchopneumonia.

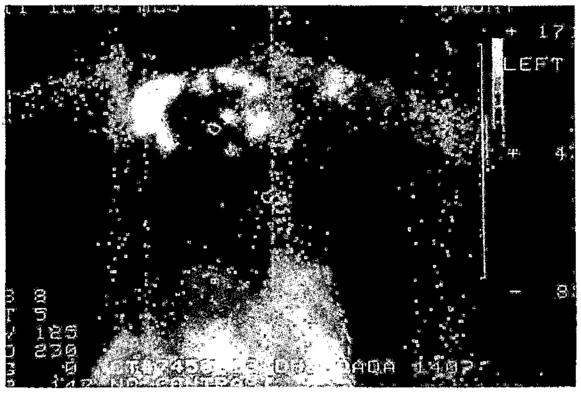

FIGURE 2. Patient 1. Computed tomogram of the sternum revealing a destructive bone lesion in the midsternum.

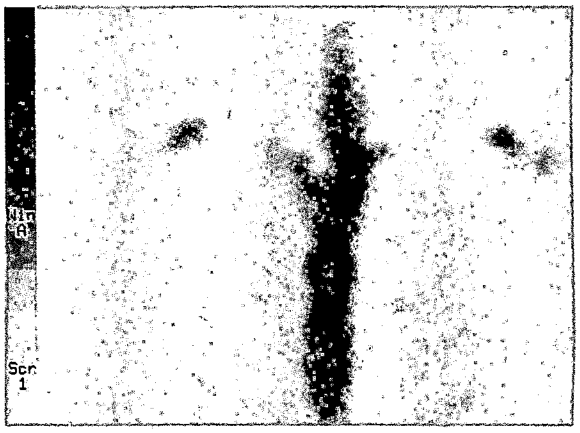

FIGURE 3. Patient 1. Isotope bone scan showing increased activity in the midsternal zone with a central cold area.

Discussion

Tuberculous osteomyelitis of the sternum is a rare clinical entity. It constitutes 1% of skeletal tuberculous cases.[2] In 1926, Wilensky and Samuels[3] reported 24 cases of sternal osteomyelitis, but paradoxically, none were tuberculous in origin. Brown and Trenton[4] described ten cases of chest wall sepsis, four with sternal tuberculous osteomyelitis. In a study of 980 patients with bone and joint tuberculosis from India, involvement of the sternum in 14 patients is reported.[5] Suba Rao et al[6] described an isolated case of sternal tuberculosis that presented with a chronic nonhealing presternal ulcer. Eight more cases of sternal tuberculosis were reported by Richter[7] in 1983. A survey of bone and joint tuberculosis from England and Wales showed two cases of sternal tuberculosis out of 198 patients.[2] In the recent report by Watts et al,[8] two more cases of sternal tuberculosis were described.

Involvement of the sternum most probably takes place secondary to bacteremia, which follows upon an infected lung or lymph nodes. While the primary focus in the first patient is not apparent, the right lung is the most likely source of infection in the second patient.

The presentation of sternal tuberculosis is variable. It may present as a painless sternal swelling (as seen in Patient 2) or as a presternal nonhealing chronic ulcer.[6] It may also present with pathologic fracture of the sternum (as in Patient 2). The latter presentation is very rare. We are aware of only one other case that had a similar clinical pattern.[8] Pathologic fracture of the sternum is reported more frequently among patients with multiple myeloma[9,10] and rarely in patients with bacterial sternal osteomyelitis.[4] Spontaneous fracture of a healthy sternum following severe cough is exceedingly rare.[11]

In endemic areas, sternal tuberculosis should be considered in the differential diagnosis of sternal neoplasms. Our first patient was operated on with the diagnosis of malignant sternal tumor. Because frozen section was not done preoperatively, total sternectomy would have been the outcome of our initial diagnosis. Therefore, if preoperative needle biopsy is not informative, frozen section should be done to avoid the risk of performing an unnecessary sternal resection.

Our first case shows the difficulty in diagnosing sternal tuberculosis, despite the extensive investigations carried out. Isotope bone scan and galium scan are sensitive tests, but they were not helpful in finalizing the diagnosis. The chances of failure to reach a preoperative diagnosis can be minimized if sternal tuberculosis is considered in the differential diagnosis and also by doing a needle biopsy. Untreated, the condition may lead to mediastinitis, as happened in our second patient. We found from our experience and that of others[4,6,8] that conservative sternal resection of involved tissues is the best treatment for sternal tuberculosis.

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TUBERCULOSIS OF THE PAROTID GLAND

Ossama Abdul Hamid, MD

نشرح هنا حالتين من سل الغدد اللعابية في النكفة. تشابهت أعراض إحدى الحالتين مع التهاب النكفية القيحي وتظاهرت الأخرى كورم حميد بطيء النمو. وظهرت على أحدهما أعراض بدنية عامة. وعلى الرغم من أن نتيجة اختبار السلّين الجلدي كانت إيجابية، إلا أنها لم تكن ذات دلالة قطعية حيث يعتبر التطعيم بعصيات «كالمت ـ غيران» إجباريا في المملكة العربية السعودية. كانت نتيجة فحص اللطاخات والمستنبتات لتقصي العصيات الصامدة للحمض سلبية. تم التوصل إلى تشخيص الحالة بالتحليل النسيجي. وثبتت أفضلية الخزع الاستئصالي على الخزع الشقي كجزء من العلاج بدون حدوث ناسور في مرحلة تالية. تمت مناقشة أعراض وعلاج تدرن الغدة اللعابية، مع مراجعة ما كتب في هذا الصدد.

Two cases of tuberculous sialadenitis of the parotid gland are reported. Presentation simulated suppurative parotitis in one case and slowly growing benign neoplasm in the other. One patient had systemic manifestations. Although skin tests were positive, they were insignificant since bacillus Calmette-Guerin vaccination is compulsory in Saudi Arabia. Smears and cultures for acid-fast bacilli were negative. Diagnosis was made by histologic analysis. Excisional biopsy as part of treatment proved better than incisional biopsy, with no fistula formation afterwards. The pathology and management of tuberculosis of the salivary glands are discussed, with review of pertaining literature.

Although cervicofacial mycobacterial infection is rare, it should be considered in the differential diagnosis of head and neck growths in general and salivary swelling in particular. This especially holds true in endemic areas like Saudi Arabia where this report originates. Cervicofacial tuberculosis can occur alone or as a part of generalized disease and salivary glands can be involved. There were frequent reports of tuberculosis of the salivary glands during the first half of the century in the Western literature, but accounts of the disease in the latter half of the century have been less frequent, indicating a decline in incidence.[1,2] Diagnosis has always been difficult to make, especially when salivary glands are involved, and necessitates a combination of all available diagnostic modalities. Two cases of tuberculosis of the parotid gland are presented with discussion of the current problems in the diagnosis and treatment of cervicofacial tuberculosis.

Case Reports

Patient 1

A 31-year-old Saudi man noticed a left preauricular mass two months prior to presentation. The swelling increased markedly and became painful during the last two weeks. Examination revealed a parotid swelling that was about 10 × 8 cm; the mass was slightly tender, partially cystic in its upper part, of limited mobility, with ill defined borders, and not attached to overlying skin which was inflamed. A small lymph node was felt at the tail of the gland. Wide-bore needle aspiration produced 10 ml of greenish pus that was negative for acid-fast bacilli (AFB). The patient had neither a past history nor recent manifestations of tuberculosis. Skin test was positive. There was a presumptive diagnosis of suppurative parotitis, and broad-spectrum antibiotics were initiated. These were given for two weeks without noticeable response. Incisional drainage yielded

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30 ml of pus. Smears and culture were negative for AFB. After a full months' course of antibiotics, neither the swelling disappeared nor did the fistula at the incision site heal. A superficial parotidectomy was therefore planned.

At operation a large abscess cavity was found that involved the upper part of the gland down to the zygoma without actual bony involvement. Histopathologic examination revealed parotid tissue infiltrated by tuberculous granulomata consisting of Langhans' giant cells, epitheloid cells, and peripheral lymphocytes together with central caseation. Antituberculous drugs were started. The incision healed well without fistula formation, and the patient did well during the year of follow-up.

Patient 2

A 32-year-old Saudi man developed a painless swelling in front of the right auricle six months prior to presentation. Examination revealed a 3 × 4 cm parotid swelling that was nontender, mobile, firm, and unattached to overlying skin. The patient had a history of pulmonary tuberculosis that had occurred a few years previously, but he failed to continue treatment. Skin test was positive. Chest x-ray study showed left apical scarring with hilar fibrosis. Fine-needle aspiration did not identify neoplasms. The differential diagnosis included mixed parotid tumor and possible tuberculous parotitis. A centrally liquefied 3 × 3 cm nodule was found at superficial parotidectomy. A small lymph node was attached to the tail of the gland. Histologic analysis showed a large area of caseous necrosis surrounded by numerous granulomata, with peripheral fibrosis separating the essentially inflammation-free parotid tissue.

Granulomata consisted of epithelioid cells, Langhans' cells, lymphocytes, and central caseation. Lymph nodes were occupied by the same granulomata. Ziehl-Neelsen stain was negative for AFB. Antituberculous drugs were started. The wound healed without fistula formation during the five-month follow-up period.

Discussion

Tuberculosis of the salivary glands is a rare condition, with the parotid gland the one most commonly involved.[2,3] Pathologic manifestation takes two forms. One form is acute inflammation with diffuse glandular swelling simulating suppurative sialadenitis (Patient 1). Infection usually involves the gland parenchyma. The second is a chronic, encapsulated indolent form that mimics a slow-growing neoplasm. This could be due to involvement of the intraparotid lymph nodes (Patient 2).

Infection reaches the salivary glands through retrograde extension along the salivary ducts via the lymphatics to the intraparotid lymph nodes, or by hematogenous spread.[3] The latter is usually associated with a more generalized tuberculosis. Tuberculosis of the salivary glands can be secondary when there is evidence of previous systemic involvement, as in Patient 2. Primary infection in the salivary glands is rare,[4,5] but our first case is considered as such.

Diagnosis of salivary gland tuberculosis is difficult. In most published series, diagnosis was not made preoperatively, even when there were associated systemic manifestations.[1,6]

Mycobacterial infection could be present despite normal chest x-ray studies, negative skin tests, negative stains for AFB, and even negative cultures. These negative results occur more commonly with atypical mycobacterial infection. Positive chest x-ray studies ranged from 60%[7] to 10%[8] in patients with tuberculous cervical lymphadenitis. Sayler et al[9] reported an 81% rate of negative chest roentgenograms in cases of atypical mycobacterial cervical lymphadenitis.[9] Unilateral gallium 67 uptake should raise the suspicion of tuberculosis.[10] However, this imaging technique together with technitium 99m pertechnetate scintigraphy, sialography, and sonography do not give pathognomonic signs for tuberculosis.[10,11]

Ziehl-Neelsen staining for AFB has been reported to be positive in 20 to 50%[6] and 44%[8] of patients with positive skin tests and histopathologic findings consistent with tuberculous cervical lymphadenitis. Positive cultures are even less reliable. Results ranged from 10%[12] to 50%[13] in patients with positive skin tests and histopathologic findings.

Skin tests are reported to be more reliable. Sensitivity ranged from 100%[7,12] to 81%.[8] However, in countries like Saudi Arabia where bacillus Calmette-Guerin vaccination is compulsory, skin tests will not be useful because they will always be positive.

Histologic analysis that reveals characteristic granulomatous reaction defines the diagnosis. Our report confirms the observation that incisional biopsy is complicated by draining fistula,[12,14,15] making excisional biopsy preferred. Excision is also part of the treatment plan. The head and neck surgeon must alert his or her pathologist to the suspected diagnosis. Fresh tissue specimens should be placed in saline and should undergo staining for AFB culture, and examination for characteristic histopathologic changes.

With the above diagnosis dilemma, clinicians have to maintain a high index of suspicion, especially in endemic areas. They must presume tuberculosis is present when systemic manifestations are evident, and combine all laboratory results with the responses to specific drugs to reach a definite diagnosis.

Treatment of cervicofacial mycobacterial infection combines surgery and drug therapy to achieve cure rates close to 100%.[7,13] Recurrence after surgery was reported to be 33% compared with an 11% recurrence after combined therapy.[6]

Superficial parotidectomy or submandibular sialoadenectomy should be followed by multidrug antituberculous chemotherapy for 18 to 24 months. Isoniazid, ethambutol, rifampicin, and pyridoxine are used in different combinations in different institutions. Culture and sensitivity testing should be done when atypical mycobacteria are suspected, since these are not generally sensitive to the usual antituberculous drugs.[16] Patients should be examined for visual acuity before starting therapy to serve as comparison in the event of complications from ethambutol. Patients' liver enzyme levels should be monitored periodically to detect any hepatotoxicity from isoniazid.

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Special Communication

ASSESSING HEALTH CARE DELIVERY IN SAUDI ARABIA

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يعالج هذا المقال بعض العوامل المتغيرة الهامة في ما يخص الرعاية الصحية في المملكة العربية السعودية، مع التركيز بشكل خاص على الرعاية الصحية الأولية. وقد راعينا فيه عوامل أخرى وهي تأثيرات العامل المالي في الرعاية الطبية، ومدى وفرة الطبيبات السعوديات والأجنبيات والاحتياجات الخاصة الناجمة عن متطلبات الحج السنوية والتي تؤثر جميعا على تقديم الرعاية الصحية في المملكة العربية السعودية. كما يصف المقال أيضا المحدودية والانحراف الناجمين عن استخدام نسبة عدد الأطباء إلى السكان دونما تحفظ كمعيار لتحديد جودة الرعاية الصحية المقدمة في المملكة العربية السعودية. اقترحنا التوصيات التي تعمل على الارتقاء بتلك النسبة الاجمالية بالاضافة إلى تلبية المتطلبات الطبية الخاصة للناس بصورة جيدة وذلك من خلال التوسع في خدمات مراكز الرعاية الصحية الأولية.

This paper deals with the some of the important variable factors relating to health care in Saudi Arabia, with special emphasis on primary health. Other aspects considered are the financial influences in medical care, the availability of female Saudi and of expatriate physicians, and the special needs imposed by the annual pilgrimage, all of which influence health care delivery in Saudi Arabia. The bias and limitations which arise from the unqualified application of the physician-population ratio in determining the quality of health care in Saudi Arabia are also described. Recommendations are made for improving this overall ratio as well as better meeting the specific medical needs of the people through expansion of primary health care services.

The physician's traditional role has been to care for and when possible cure the sick, to stem the progression of disease, to minimize damage, to relieve pain and suffering, and to comfort at all times. These are major aspects for which physicians are trained. There is, however, another increasingly important role for physicians, that of the educator who can facilitate the early recognition and prevention of disease by promoting health-fostering attitudes.

As the practice of medicine has become increasingly complex and effective, physicians no longer single-handedly do everything required to treat their patients, much less take on all aspects of comprehensive care. They rely on a variety of trained personnel–nurses, laboratory technicians, radiographers, physiotherapists, pharmacists, and so forth.

This means that in determining the needs for the efficient delivery of health care, two questions must be answered. First, how many of each category of health care personnel does a country need, in the short and long term? And second, what proportions will best meet the social mix and achieve the greatest economic efficiency? The answers depend on a steady flow of information about, and adequate appraisal of, health conditions in the country, the nature and magnitude of illness and their determinants, and the extent to which health requirements are part of overall socioeconomic development.

One way to assess health care delivery is through ratios. In Saudi Arabia for the year 1407H (1987G), the physician-population ratio was 1:582; the nurse-population ratio, 1:276; the bed-population ratio, 3.3:1,000; and the primary health care center-population ratio, 1:7774. These are important statistics and indicate that Saudi Arabia has made great strides in the development

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of its health care delivery system.

A physician-population ratio, which is a popular tool for assessing the quality of health care, is not by itself an accurate indicator of the health status of a country's population, although it may roughly reflect the level of development. Underdeveloped nations can have a ratio as low as 1:12,346 (Sri Lanka, 1983), while developed nations can have a ratio of 1:500 (U.S.A., 1982), but the ratios do not always correlate directly with development[1] (Table 1).

Other factors that influence the health status of a population include the quality of housing, personal hygiene, diet, sanitation, and level of education. A major drawback of the physician-population ratio is that a higher ratio is taken to mean better health care, which is not necessarily so. The quality and experience of practitioners also must be taken into consideration, remembering that good health care is that which is readily accessible at a low cost.

TABLE 1. *Physician-population ratios for other countries.*

Country	Year	Physician-population ratio
Argentina	1980	1:603
Brazil	1980	1:1170
Canada	1983	1:603
Colombia	1985	1:1548
Cuba	1985	1:439
Egypt	1985	1:655
India	1985	1:3000
Mexico	1985	1:810
Pakistan	1985	1:3690
Phillipines	1982	1:1667
Republic of Korea	1984	1:1447
Sri Lanka	1985	1:12346
United States of America	1982	1:500

TABLE 2. *Physicians in Ministry of Health according to nationality, 1987 (1407H).*

	Nationality		
Medical facility	Saudi	Non-Saudi	Total
Hospitals	960	6643	7603
Primary health care centers	29	3224	3253
M.O.H. headquarters	86	384	470
Total	1075(9.5%)	10,251(90.5%)	11,326

Ratios can provide useful information when used in the correct context. The aim of this paper, therefore, is to discuss some of the limitations of the physician-population ratio, and to examine variables relevant to the health care delivery system, with special emphasis on Saudi Arabia.

Variables Influencing Quality of Health Care

Demography

Although cities generally have higher physician-population ratios, they do not necessarily have more general practitioners per capita,[2] and it is the general practitioner who provides primary health care. Many physicians in urban areas are specialists whose expertise is not really relevant to the general population, but their numbers augment the physician-population ratio.

In a country like Saudi Arabia, where primary health care is a high priority, the concentration of physicians in urban areas is for this reason misleading in assessing the availability of general health care. In this context, only general practitioners should be considered in a count of physicians in urban areas, because only this figure can accurately portray the adequacy of primary health care delivery.

Quality

Ratios are used to determine whether there is a sufficient number of physicians and to provide a basis of comparison with data from other parts of the world. However, ratios and other such statistics cannot supply information about the quality of the physicians serving the population. For example, in Saudi Arabia, a large proportion of the medical manpower is made up of expatriates of various nationalities (Table 2). Not all are of the same quality and training, and whilst many are outstandingly well qualified, some are undertrained. A large proportion do not speak Arabic, making communication with patients difficult. Expatriate personnel are often transient and this affects the long-term development of a patient-physician relationship. All of these factors have an important bearing on the quality and continuity of care.

To assess the quality of a practitioner's care, many factors must be considered. Number of years and quality of training, standing in class, CME credits earned, society affiliations, board certification and the granting board, number of procedures performed and outcome (in the case of surgeons)–these are just some of the factors that must be considered when examining the ability of the practitioner and the quality of care, and statistics such as ratios cannot reflect this.

To evaluate other aspects of the delivery system, even more factors must be considered. These include the number of hospitals and beds in each, the extent of the population served and the geographic area covered, emergency services, availability of supplies, and numbers of other paramedical personnel, just to mention a few.

Financial Influences

The governmental sector of health care in Saudi Arabia provides mostly free service. The private sector performs an important function that is payable. The method of payment for medical care has a powerful influence in what individuals and professionals do; and is an important consideration in an assessment of health care.

There are two basic types of payment: payment which encourages service to the individual (direct or item of service payment) and payment which encourages services to groups as a whole.

Individual Service: Payment which encourages service to the individual includes payment made by the patient directly to the practitioner on a fee-for-service basis, or fee-for-service paid by a state or private insurance scheme.

The advantages to payment for individual services include (1) encouragement of personalized service; (2) high job satisfaction among practitioners, because they get paid according to the amount and quality of their work; and (3) availability of patient criticism and feedback, and therefore a direct say in the kind of care received.

The disadvantages to direct payment approach include the following. (1) It does not cultivate good health education and discourages preventive medicine. (2) Patients are left to "shop around" for medical care, often with little guidance or knowledge concerning the type of care they should be seeking. (3) Specialists under this scheme are inclined to congregate in urban areas, where the numbers of patients and income are greater, and there are also few controls in determining their numbers and location, to the detriment of the rural population. (4) Because the service is open ended, overservicing of the patient's needs can occur.

Payment Based on Service to a Group: Payment which encourages service to a group as a whole is of three types: sessional, capitation, and full-time salary. There are four advantages to this approach: (1) it fosters a community health team approach; (2) it encourages preventive medicine and good health education; (3) because of this preventive approach, patients can be cared for within their community and the number and extent of hospitalizations are decreased; and (4) salaries can be adjusted to attract physicians to outlying areas, thus controlling the distribution of practitioners.

Disadvantages of this system include the discouragement of personalized service, lack of financial incentives based on quality and amount of service, and the possibility that patients may be underserviced.

It is also important to define the numbers of physicians in the government and private sectors (Table 3). The importance of the private health sector in providing health care in Saudi Arabia can be estimated by the magnitude of its bed capacity: in 1987G (1407H) it supplied 13.5% of the total hospital beds.

TABLE 3. *Health services supplied by different sectors in Saudi Arabia 1407H (1987G).*

Sector	Beds (%)	Physicians (%)	Nurses (%)	Technicians (%)
Ministry of Health	25,902 (69.3)	11,326 (59)	25,987 (64.1)	12,793 (65)
Other government sectors	6,437 (17.2)	3,654 (19)	8,551 (21.1)	4,282 (21.8)
Private sector	5,091 (13.5)	4,222 (22)	5,983 (14.8)	2,591 (13.2)
Total	37,358	19,202	40,521	19,666

TABLE 4. *Professional medical employees in Ministry of Health 1987 (1407H) according to nationality and sex.*

	Saudi		Non-Saudi		Total
	M	F	M	F	
Physicians	680	395	8492	1759	11,326
Pharmacists	122	10	234	116	482
Chemists	37	9	57	26	129
Microbiology specialists	11	9	23	11	54
Nurses	1120	–	3594	20,187	24,901
Surgical assistants	213	1085	110	198	1606
Laboratory assistants	323	2	1451	725	2501
Radiology assistants	366	32	1155	175	1728
Pharmacy assistants	628	2	1708	358	2696
Anesthesia assistants	209	–	136	38	383
Sanitary inspectors	803	–	997	3	1803

Medical Assistants and Other Medical Personnel

Physician-population ratios do not take into account other personnel such as pharmacists, nurses, laboratory assistants and so on (Table 4). Medical auxiliaries include nurse practitioners, physicians' assistants, pediatric assistants, family health workers, and midwives. In the U.S.A, medical auxiliaries perform a major role in the delivery of health care, and relieve physicians of many responsibilities that formerly fell to them. The use of medical auxiliaries as physician extenders improves the access of patients to health care. Thus, the meaning of physician-population ratios has changed as physicians have come to serve increasingly as leaders of teams of health care professionals, and such ratios must therefore be interpreted in the light of the extent and quality of such auxiliary services. Table 5 shows the number of physicians and nurses working in the Ministry of Health during the period 1978-1987.

Medical Specialization

Overall physician-population ratios do not differentiate among the numbers of practitioners in various specialties, and cannot accurately show whether there is an over or undersupply. For example, in the U.S. it is generally acknowledged that there is an oversupply of surgeons, and if these doctors are counted into the physician-population ratios, the delivery of general health care looks better than it actually is.

Health care planners must project demands based on accurate statistics to ensure correct numbers of physicians representing different specialties. Table 6 shows the total number of physicans working in the Saudi Ministry of Health categorized by specialty for the year 1407H (1987G). The total number of physicians in the Ministry of Health (11,326) yields a ratio of one physician to 582 people. However, a ratio roughly double (1:1013) results when only the 6513 general practitioners are considered.

Women Physicians

In a country such as Saudi Arabia it is important to distinguish between the numbers of male and female health care workers, including physicians and paramedical personnel, because of the Muslim customs which dictate greater segregation of the sexes and make it preferable for female patients to be examined by female physicians. Table 4 shows the male and female distribution of

TABLE 5. *Physicians and nurses in hospitals of the Ministry of Health, 1398–1407 A.H. (1978–1987 G).**

Year	No. of nurses	No. of physicians
1398	7,137	3,558
1399	8,136	4,064
1400	8,776	4,550
1401	11,599	5,585
1402	13,400	6,649
1403	16,809	8,565
1404	19,641	9,966
1405	25,964	12,199
1407	25,986	11,326

*From reference 7.

TABLE 6. *Number of physicians working in the Ministry of Health by specialization (1987).* *

Specialty	No.
General practitioners	6,513
Dentists	868
Internal disease specialists	431
Surgeons	406
Pediatricians	421
Obstetricians and gynecologists	484
Ophthalmologists	200
Neurologists and psychiatrists	137
Dermatologists and venerologists	107
Otorhinolaryngologists	169
Radiologists	174
General health and tropical medicine	81
Bone diseases	196
Urologists and nephrologists	115
Pathologists	286
Chest physicians	101
Anesthesiologists	323
Others	314
Total	11,326

*From reference 8.

Saudi and non-Saudi medical personnel in 1987.

The Pilgrimage

During the annual Haj pilgrimage the health care services of Saudi Arabia are particularly strained. Between 1970 and 1982 the number of pilgrims doubled from one to two million, and the number from outside the country rose from 431,000 to 853,000. Thus, in considering the quality of health care delivery, one must note that the physician-population ratio is altered by the large influx of pilgrims.

Any estimate of health manpower must consider the special problems posed by the annual pilgrimage, not only in terms of the number of people but also the special health problems associated with this group of people.

Expatriate and Saudi Physicians

During 1987, expatriate physicians constituted 90.5% of physicians in the Ministry of Health (see Table 2). With a trend toward reducing the number of expatriate personnel and replacing them with Saudi personnel, close consideration must be given as to how this process will affect the overall ratio and how to effect a smooth transition toward the development of a dominantly Saudi corps of health care personnel.

The enrollment in Saudi medical schools increased from 276 in 1975 to 3,000 in 1985, but these numbers do not take into consideration the quality of the education, the postgraduate specialty areas pursued, the number of Saudis receiving medical education abroad, and other qualitative factors that numbers cannot describe.

Primary Health Care Approach

Until 1979, the emphasis of health services in the Kingdom of Saudi Arabia was primarily on cure and not prevention. Such care was provided by hospitals and dispensaries. Many dispensaries were not open full-time and over half were run by auxiliaries.[3-6]

Since 1980, the Ministry of Health has gradually implemented the primary health care approach. The health offices and maternal child health centers were abolished and their functions incorporated into those of primary health care centers, which have increased yearly in number so that now such care extends throughout the Kingdom. As of 1987, 1438 primary health care centers were in operation. In addition, the Ministry of Health adopted the following strategies:

1. Expanding and extending the delivery of comprehensive health services with optimum quality, to be accessible to all people, through primary, secondary, and tertiary levels.
2. Strengthening the link between these three levels of health service.

Newly trained primary care physicians can help meet the primary care needs of the population, especially in rural, bedouin, and inner-city areas. They can deliver high-quality care, substantially increase the productivity of the physician's practice, and enhance preventive services to patients. This is the most acceptable method of improving the physician-population ratio.

Recommendations and Conclusions

It is a cardinal principle that the manpower pattern in any health service must be governed by what countries can afford, rather than by what health authorities would like.

What ratio of different grades of health personnel will best utilize the limited budget allocated for a given district? The answer should be reflected in the grades and numbers of personnel being trained.

The aim is access to health care for all by the year 2000 through the further development of the primary health care system, which requires careful analysis of manpower needs. To ensure an adequate supply of appropriately trained primary care practitioners, there must be a substantial increase in the number of residents in primary care training programs. It is really the primary care physician who manages the great majority of health problems.

There must also be greater use of the team approach, with good exposure to clinical experience. Instruction in epidemiology and the behavioral and social components of patient care is also necessary. Medical students who currently rotate predominantly among in-hospital services should also serve in a primary care setting. Interdisciplinary training should be promoted so that health professionals can serve in a collaborative delivery system.

Medical schools should be affiliated with at least one primary care residency program. Extensive and imaginative initiatives are needed to orient medical education sufficiently toward primary care. Such initiatives will generate unavoidable inconveniences and costs for medical schools, but ultimately the benefits from the quality of primary care training will outweigh the cost of change.

More accurate data and information about the use and accessibility of primary care services must be obtained to ensure effective health planning and policy making.

An efficient nursing workforce is essential to guarantee equal access for all to quality health care at a reasonable cost. Table 5 shows the increase in nursing and physician personnel from 1398H to 1407H (1978-1987G). Although the statistics are encouraging, one must bear in mind that these numbers include a large proportion of expatriate personnel.

In addition to decreasing the over-reliance on non-Saudi physicians, health authorities must also find suitable incentives for urging Saudi females to enter the nursing profession. The reasons for the evident deficiency of Saudi nurses must be investigated and solutions sought.

There must be an active and continuous program to monitor the number of physicians in different specialties and the geographic distribution of all physicians, nurses, and auxilliaries.

These measures will create a suitable physician-population ratio, with a cost-effective and efficient health service as the ultimate benefit.

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Case Reports

BEHCET'S DISEASE WITH RENAL AMYLOIDOSIS: REPORT OF A CASE FROM JORDAN WITH REVIEW OF THE LITERATURE

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In the description of the disease carrying his name, Behcet[1] reported a triad of aphthous stomatitis, genital ulcers, and ocular inflammation. It was found later that Behcet's disease can affect multiple systems with mucocutaneous, ocular, intestinal, articular, vascular, pulmonary, and neurologic involvement.[2,3] The kidneys have been reported to be infrequently affected[4,5] and some authors have stated that renal involvement does not occur in Behcet's disease.[6] In our review of the literature, we found that renal involvement is not as uncommon a finding as was once thought, and both amyloid and nonamyloid renal lesions have been recently reported with increasing frequency.

We report a case of Behcet's disease associated with nephrotic syndrome due to renal amyloidosis and discuss briefly the relevant literature.

Case Report

A 34-year-old man was admitted to Jordan University Hospital in November 1978 because of pain and swelling of the whole left lower limb of a few days' duration. On further questioning, the patient admitted that, for the past ten years, he had had recurrent attacks of conjunctivitis with oral, genital, and scrotal ulcerations, as well as swelling of the right leg a few years before the current presentation. Family history for similar conditions was negative. On physical examination, the general condition of the patient was fair. His left lower limb was painful and edematous with a few dilated superficial veins, while the right leg was mildly edematous.

Slit lamp examination showed old anterior uveitis with posterior synechiae, and funduscopy revealed pale retina with narrowed arterioles. Pustules were noticed at the sites of vein punctures. Intradermal injection of 0.1 ml of sterile normal saline solution produced a pustule at the site of injection (positive pathergy test). Remaining findings from the physical examination were unremarkable.

The clinical diagnosis of Behcet's syndrome was considered and the following laboratory investigations were done. Urinalysis showed proteinuria with 24-hour total urine protein of 4.5 g/d. Total serum protein was 64 g/L; albumin, 22 g/L; blood urea, 12.14 mmol/L; serum calcium, 2 mmol/L; phosphorus, 1.6 mmol/L; and serum creatinine, 97.24 μmol/L. Serum electrolytes, glucose, immunoglobulins, cholesterol, and liver enzyme levels (SGOT, SGPT, and alkaline phosphatase) were all within normal limits. Tests for hepatitis B surface antigen, cryoglobulins, lupus erythematosus cells, antinuclear antibody (ANA), and rheumatoid factor were all negative. Prothrombin and partial thromboplastin time were normal; the fibrinogen level was 4.5 g/L; antithrombin III was 60%; and euglobulin lysis time with and without stress showed decreased fibrinolytic activity. The erythrocyte sedimentation rate was 115/h; hemoglobin, 135 g/L; white blood cells, 8.6 × 10^9/L; and platelets, 250 × 10^9/L. C_3 and C_4 complement components were normal. Bipedal venography showed evidence of thrombosis in the deep system of both legs and the left femoral vein. Chest x-ray study, barium meal and follow through, and intravenous pyelography were unremarkable.

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Percutaneous needle kidney biopsy was done and showed renal amyloidosis of moderate degree involving the glomeruli and the walls of blood vessels with focal interstitial fibrosis and inflammation (Figure 1). Congo red stain showed typical apple green birefringence under polarized light.

The patient was discharged on the following medications: prednisolone, hydrochlorothiazide, phenformin, and colchicine, and was followed in the outpatient clinic until March 1979. He was lost to follow-up for 30 months, but was readmitted in October 1981 because of generalized weakness, shortness of breath, dizziness, and deterioration of vision. The major findings on physical examination were generalized edema and bilateral pleural effusion. Laboratory data showed deteriorating renal function: urea was 50.3 mmol/L which progressed to 111.4 mmol/L and creatinine was 556.9 μmol/L which rose to 1317.2 μmol/L. Total serum albumin was 11 g/L and hemoglobin was 84 g/L. Urinalysis showed proteinuria, and 24-hour urine protein was 12 g. A second percutaneous kidney biopsy was undertaken and showed extensive amyloid deposits in the glomeruli which became totally obsolescent, with severe tubular atrophy and marked interstitial fibrosis and inflammation (Figure 2). Tissue submitted for electron microscopy after fixation in glutaraldehyde proved to be from the medulla. Nevertheless, many amyloid fibrils with their typical haystack pattern were seen in the walls of blood vessels, around tubules, and free in the interstitium (Figure 3).

The patient was treated with diuretics, albumin infusion, colchicine, and prednisone. He was placed on peritoneal dialysis and died one month after his last admission.

Discussion

The diagnosis of Behcet's disease can be made if the patient has at least three of the four major symptoms (oral aphthae, genital aphthae, skin

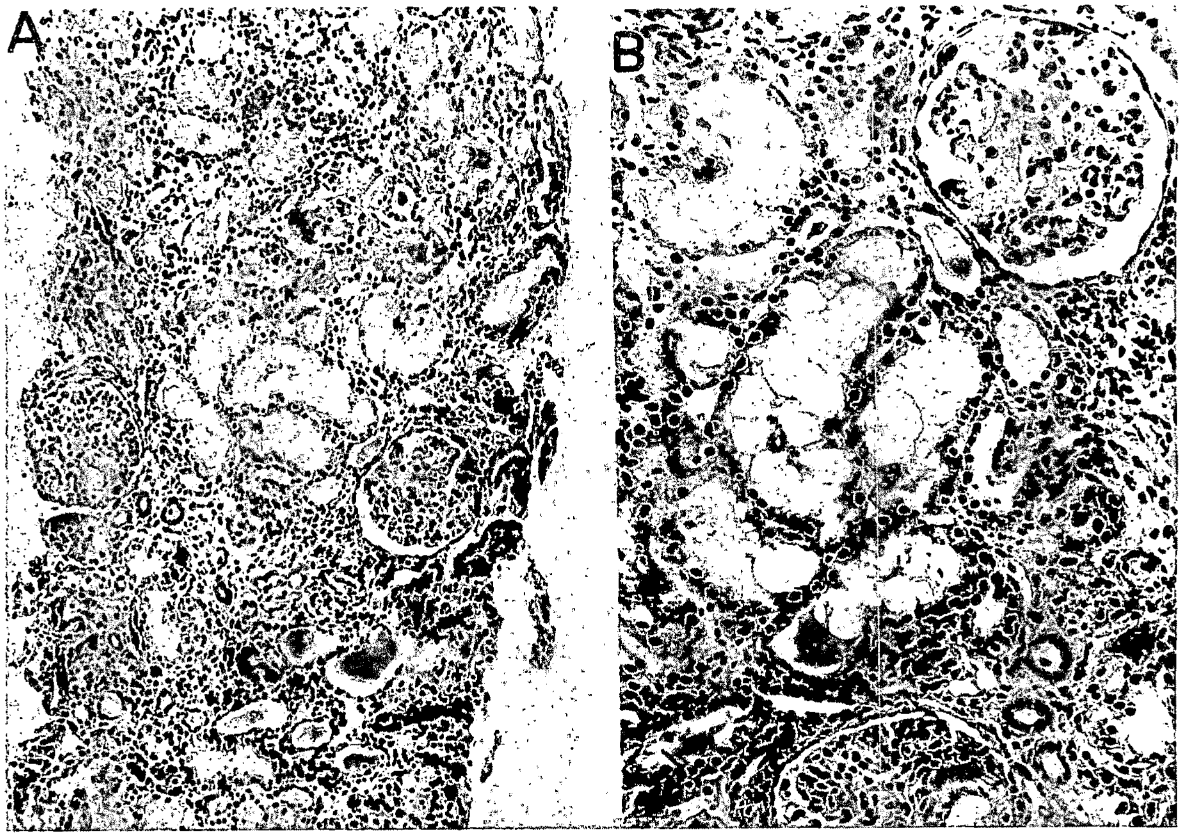

FIGURE 1. First kidney biopsy. (A) Low magnification view. Note partial preservation of glomeruli, focal interstitial fibrosis and inflammation, and tubular atrophy and casts. (H&E; original magnification, × 75.) (B) High magnification view. Note amyloid deposition in afferent arteriole and mesangium with preservation of many capillaries. (H&E; original magnification, × 225.)

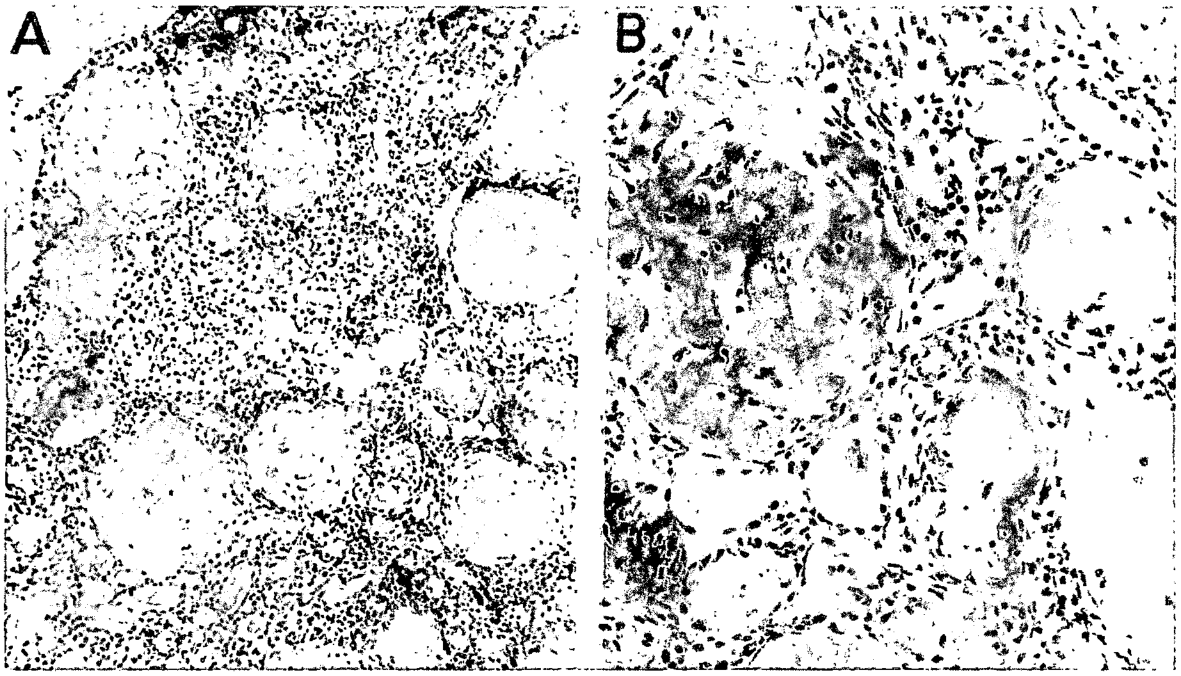

FIGURE 2. Second kidney biopsy. (A) Low magnification view. Note marked involvement of glomeruli by amyloid deposits, with severe tubular atrophy and heavy interstitial inflammation. (H&E; original magnification, × 75.) (B) High magnification view. Obsolescence of glomeruli due to heavy amyloid deposits is evident. (H&E; original magnification, × 225.)

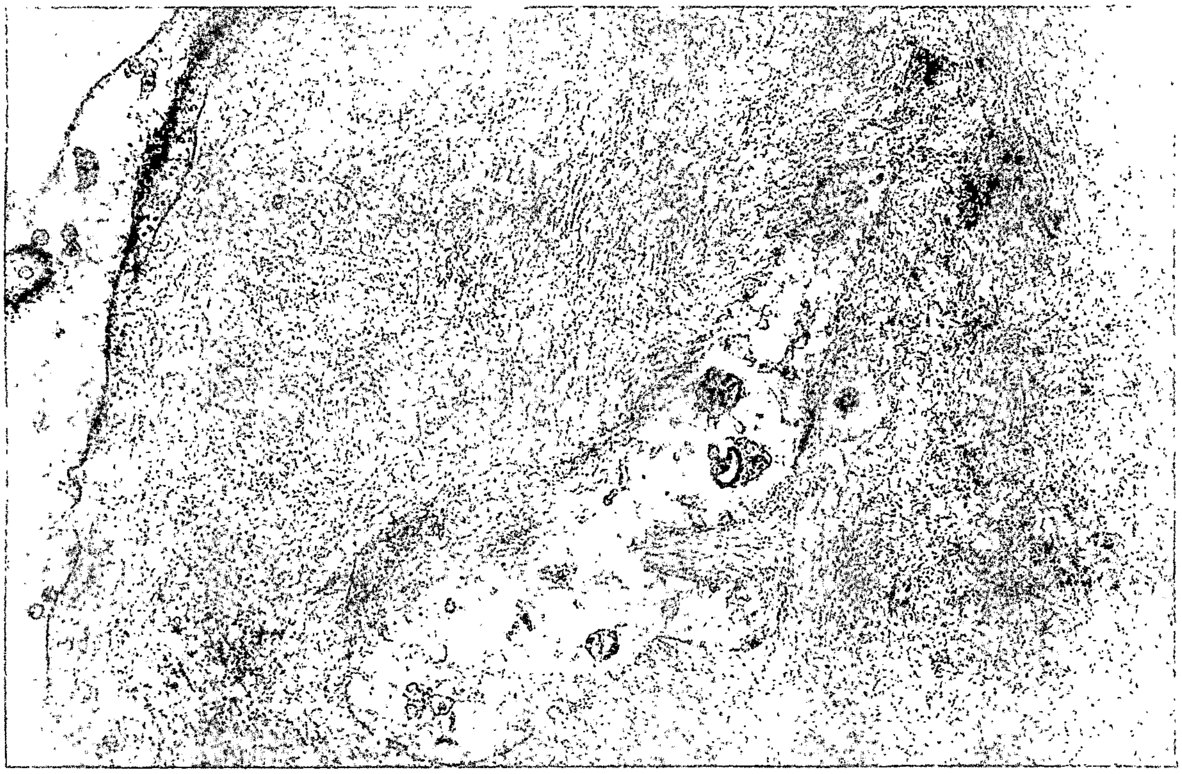

FIGURE 3. Electron micrograph of blood vessel wall from the medulla showing amyloid fibrils with typical haystack pattern. (H&E; original magnification, × 16,000.)

lesions, and uveitis) or two major symptoms and at least two of the minor symptoms (arthritis, thrombophlebitis, cardiovascular lesions, gastrointestinal lesions, central nervous system lesions, renal involvement, and positive family history).[8] Our patient had four of the major and two of the minor symptoms.

Although circulating antigen-antibody complexes have been detected in Behcet's disease,[9,10] involvement of the kidneys in this multisystemic disease has been reported infrequently.[4,6] The frequency of renal involvement is variable from one series to another. Thirteen of 65 Japanese patients (20%) had urinary abnormalities.[2] Only two of 38 patients (5.2%) with Behcet's disease who were studied at Guy's Hospital, London, had renal abnormalities.[11] In one study,[12] 14 of 51 patients (27%) had proteinuria, hematuria or both, but another study[6] of 41 patients from the same population revealed no renal involvement. Among 268 patients from Turkey, only eight had renal amyloidosis.[7]

Nestor et al[13] from Romania were the first to document fully the association of Behcet's disease with renal amyloidosis. Their two patients were 23- and 38-year-old men with intense proteinuria. They later reported on another three male patients:[14] Oriental Jews and a Palestinian Arab with minimal to severe proteinuria. Twelve patients were reported from Turkey,[7] two patients from Spain,[15,16] and one patient each from Italy,[17] Greece,[18] Tunisia,[19] the U.S.,[20] and Japan.[21]

The cumulative data on 24 cases of Behcet's disease with amyloidosis reported in the world literature until 1987 were reviewed and tabulated by Dilsen et al.[7] Twenty-two of the patients were males, and only two were females. This reflects the general preponderance of males with Behcet's disease. The ethnic distribution of the patients is interesting since 20 were from Mediterranean countries, namely Turkey, Occupied Palestine, Italy, Spain, and Tunisia.

The clustering of cases in Mediterranean[6,7] and Far Eastern countries,[4] the occurrence of the disease in several members of the same family,[6,8,22] and the increased incidence of HLA-B5 in patients with Behcet's disease[23,24] all suggest that environmental and genetic factors play an important role in the pathogenesis of the disease.

Based on the descriptions in the literature, renal lesions in Behcet's disease can be one of three types: amyloidosis,[7] glomerulonephritis,[5,25-31] and glomerular deposits of immunoglobulins and complement proteins.[32,33] Patients may present with microscopic hematuria, proteinuria alone, or proteinuria with hematuria.[11]

There have been several single case reports describing Behcet's disease in association with focal glomerulonephritis[5,25,26,30,31] or diffuse proliferative glomerulonephritis of variable severity[27-29] with or without crescent formation. Small scattered deposits of C_3, IgA and/or IgG, and Clq were seen by immunofluorescent microscopy in the mesangia and capillary basement membranes in 11 patients reported by a group of French workers.[32,33]

The relationship between amyloidosis and Behcet's disease has not been clarified.[7,14] Although an immunologic etiology has been suggested,[34,35] no immunologic evidence was found to explain the occurrence of renal amyloidosis.[17] Furthermore, in none of the cases in which there were deposits of complement proteins or immunoglobulins, did renal amyloidosis develop.[32,33] Some authors have suggested that renal amyloidosis may be an intrinsic symptom of the disease and therefore should be considered as another minor manifestation,[7,13] while others have considered amyloidosis a complication of the chronic sepsis seen in some patients with Behcet's disease, because it occurred two to 11 years after Behcet's disease was initially diagnosed.[16,17]

Complement C_3 and C_5 serum levels in our patient were consistently normal, serum cryoglobulins were undetectable, and there was no evidence of other conditions that are usually associated with the development of amyloidosis[36] such as chronic infectious diseases, rheumatic disorders, and familial Mediterranean fever. Familial Mediterranean fever is an important cause of amyloidosis in several Middle Eastern countries, including Jordan.[37]

Although Behcet's disease is not rare among Arabs, there have been only a few reports of the disease among this population. A study of 60 patients from Iraq did not provide data on renal involvement.[38] Another report from Saudi Arabia described 14 patients from two unrelated families, but no associated kidney disease was documented.[39] In a recent study of 46 patients with Behcet's disease conducted in Saudi Arabia, only one patient had renal involvement. Kidney biopsy revealed mesangial proliferative glomerulonephritis.[40] From Tunisia, a clinical and pathologic study of 55 patients with Behcet's disease was presented at an international congress on the disease.[41] A Tunisian patient who suffered renal amyloidosis was later reported on.[19]

Colchicine has been beneficial in treating some forms of secondary amyloidosis,[42] and produced clinical improvement in three reported cases of secondary amyloidosis in Behcet's disease.[7,9] Our patient received colchicine but did not show any improvement, and progression of amyloidosis was not slowed. This is probably due to initiation of colchicine therapy late in the disease and to noncompliance on the part of the patient.

We conclude that it is imperative to study renal function in all patients with Behcet's disease to exclude renal involvement by amyloid or glomerulonephritis, both of which could lead to renal failure and death.

Acknowledgment

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FAMILIAL TYPE E BRACHYDACTYLY IN A SAUDI FAMILY: A CASE REPORT WITH DISCUSSION OF THE DIFFERENTIAL DIAGNOSIS

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Shortening of the digits is one of the important and commonly encountered skeletal dysplasias.[1-3] Short hands or feet may be part of a generalized disorder or due to metacarpal or metatarsal shortening. The presence of digit shortening, however, is usually nonspecific and, by itself, may not be helpful in diagnosing the specific syndrome except after excluding the other dysplasias. A Saudi family with type E brachydactyly is reported and the differential diagnosis is discussed.

Case Report

A 19-year-old Saudi woman was referred to King Khalid University Hospital for investigation of her short stature. Her parents indicated that her stunted growth had been noted from early childhood. Her menarche occurred at age 14. There was no history of tetany, convulsions, or fainting. Her mental development was normal. Family history revealed the presence of short stature, which included her parents and all of her three sisters and four brothers. Her father, one of her brothers, and one of her sisters, in addition to short stature (heights: 155, 153, 145 cm, respectively), also had short fourth and fifth metacarpal and metatarsal bones (Figures 1 and 2). There was no family history of mental retardation, tetany, convulsions, or syncope.

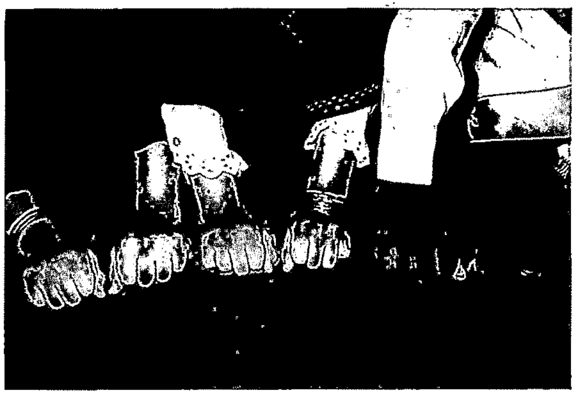

FIGURE 1. Hands of three members of the family, showing the typical metacarpal abnormality.

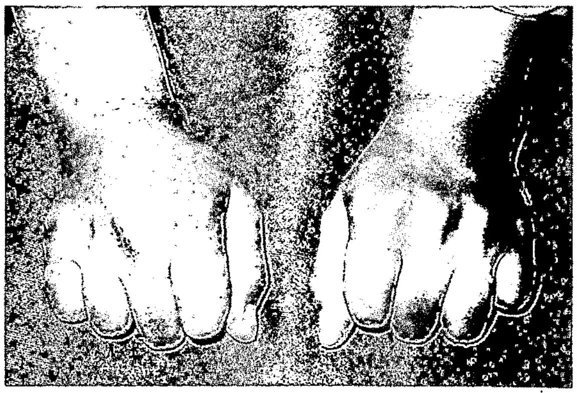

FIGURE 2. Short metacarpals (more marked on the right) with dimples instead of knuckles.

On examination, the patient's height was found to be 142 cm, and weight, 43.6 kg. Her face was not rounded. Her neck was not stocky and her secondary sexual characteristics were appropriate for her age. Skin findings were unremarkable. Examination of the skeletal system revealed short fourth and fifth metacarpal (more marked on the right side) and metatarsal bones.

Findings from physical examination of the other family members were otherwise unremarkable. There was no evidence of calvarium thickening. Her calcium and phosphorus levels were 2.33 (reference intervals, 2.1-2.6) mmol/L and 1.4 (refer-

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ence intervals, 0.8-1.4) mmol/L, respectively. Her parathyroid hormone (PTH) mid-region level was 32 (reference interval, 5-45) pmol/L. X-ray studies of her hands revealed the short metacarpal bones (Figure 3). The PTH stimulation test was not performed because PTH was unavailable in the Kingdom. Calcium, phosphorus, and PTH levels of the family members with similar dysmorphic features were within normal limits.

Discussion

The term "brachydactyly" refers to shortening of digits resulting from maldevelopment. Shortening of the metacarpal bone, especially the fourth, may be a nonspecific, isolated finding in some bony dysplasias. Other short metacarpal bones, especially the third and fifth, have been described in many syndromes which are characterized by their own specific phenotypic features.[4]

In our affected family, it is evident that the only phenotypic features were brachydactyly and short stature. The familial pattern of these features will also narrow the differential diagnosis to pseudohypoparathyroidism (PH), pseudopseudohypoparathyroidism (PPHP), and brachydactyly type E. However, it is generally accepted that the mode of inheritance of PH/PPHP follows an X-linked dominant pattern. When the transmission is autosomal dominant, as in this family, the likely syndrome is brachydactyly type E.[2,5,6] However, a few kindreds with PH/PPHP with male-to-male transmission have been described.[5] Indeed, Graudal et al[6] have proposed that PH, PPHP, and brachydactyly type E may, in fact, represent variable expressions of the same trait or allelic traits.

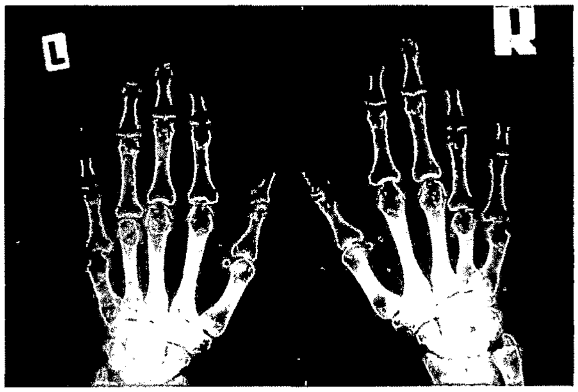

FIGURE 3. Short metacarpals, more marked on the right.

The different forms of dominantly inherited brachydactyly syndromes were initially classified by Bell in 1951 and Bell's classification was modified by Temtamy and McKusick[7] in 1969. Currently, the brachydactyly syndromes are classified into nine types: A1, A2, A3, A4, A5, B, C, D, and E (Table 1). The type A brachydactylies are characterized by shortened or absent (as in type A5) middle phalanges. In type B, there is, in addition, shortening or absence of the terminal phalanges and symphalangia. Type C is characterized by deformity and shortening of the middle and proximal phalanges of the second and third fingers. In type D brachydactyly (stub thumb), there are broad and short terminal phalanges of the thumbs and big toes. Type E is distinguished by the shortened metacarpals and metatarsals, especially the fourth and fifth. Short stature, as in our family, has also been described in this brachydactyly.[8] Table 1 summarizes the main features of the brachydactylies as well as some of their less commonly encountered skeletal anomalies.

TABLE 1. *Brachydactyly syndrome.*

Type	Main features
A–1	Short middle middle phalanges. Dysplasia of femoral heads.
A–2	Short middle phalanges of 2nd finger and toe. Radial deviation of terminal phalanx of the 2nd finger.
A–3	Shortening, flexion, and curving of 5th finger.
A–4	Short middle phalanges of 2nd and 5th fingers. Absent lateral four toes.
A–5	Absent middle phalanges. Dysplasia of nails. Duplication of the terminal phalanx of the thumb.
B	Short middle phalanges. Absent or shortened terminal phalanges. Dystrophy of nails of 2nd and 5th fingers. Broadening or partial duplication of terminal phalanx of thumbs. Syndactyly.
C	Short, deformed proximal and middle phalanges of 2nd and 3rd fingers.
D	Short, broad terminal phalanx of the thumbs and big toes.
E	Short metacarpals and metatarsals. Short stature. Short phalanges, especially of the thumb and big toe and the middle phalanx of the 5th finger. Cone-shaped epiphyses in hand.

Conclusion

The autosomal dominant transmission of the brachydactyly trait in our family suggests that it is type E. This appears to be the first documentation of familial short stature with brachydactyly in a Saudi family and physicians should be alert to these and allied syndromes in the Saudi population.

Family members and newborn babies in families with type E brachydactyly should be screened for PH, for the reasons raised by Graudal et al.[6] Early diagnosis and treatment of hypocalcemia in affected members may prevent serious complications such as convulsions and even mental retardation.[6]

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NONOBSTRUCTIVE LARGE BOWEL DISTENTION (OGILVIE'S SYNDROME)

Mohammed H. B. Khoshim, FRCS(C)

Ogilvie's syndrome is an acute dilatation of the large bowel without organic obstruction.[1,2] It is due to an imbalance between the sympathetic and parasympathetic nerve supply of the large bowel.[1,3,4]

Many medical and surgical conditions have been associated with the syndrome.[5-7] Most cases can be managed conservatively[4,8] or with colonoscopy,[8-11] and only a minority require surgery. The clinical picture and management of five cases of Ogilvie's syndrome seen at King Khalid University Hospital over a two-year period are described.

Case Reports

Patient 1

A 45-year-old staff surgeon was admitted to the orthopedic floor because of severe backache and was placed in traction. Thirty-six hours later he complained of discomfort throughout the abdomen, with severe distention and inability to pass gas. Vital signs were stable. The abdomen was slightly tender in all areas. Bowel sounds were absent and a tympanic sound was heard on percussion.

Plain films of the abdomen showed a dilated large bowel, especially the cecum. Nasogastric tube suctioning was started, the patient was given nothing orally, and more effective analgesia was administered for the backache. Within 72 hours the patient was feeling much better, started to pass gas, and the distention resolved (Figure 1).

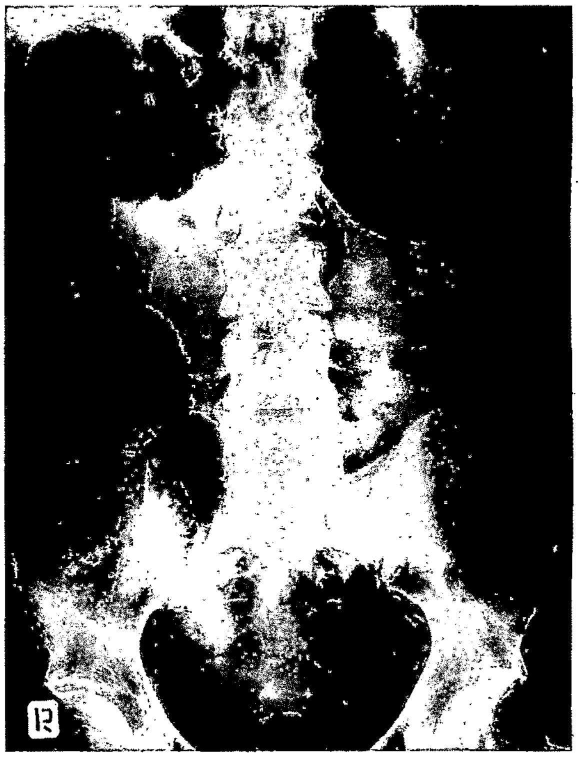

FIGURE 1. Plain x-ray study in Patient 1 showing distention of large bowel.

Patient 2

A 70-year-old woman with right hemiplegia was admitted because of a suspected large bowel obstruction. The patient was dehydrated and slightly confused. Her abdomen was distended and tympanic with no tenderness, bowel sounds were absent, and she was unable to pass gas. Laboratory investigation showed hypokalemia at 2.1 mmol/L. Plain x-ray study of the abdomen showed a distended large bowel. After correction of the dehydration and hypokalemia as well as nasogastric suction, her condition improved considerably over 48 hours. Barium enema subsequently showed no pathology.

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Patient 3

A 30-year-old man was admitted with fracture of the L1 vertebra suffered in a traffic accident. Abdominal tap was negative. He had no other injury. Two days after admission, he began to complain of slight abdominal discomfort, inability to pass gas, and distention of the abdomen.

On examination, vital signs were stable and the abdomen was distended and tympanic, with no tenderness. Plain x-ray study of the abdomen showed a distended, large bowel. He was put on nasogastric suction and increased analgesia and closely observed. His condition improved slowly over the next 72 hours, when he was able to pass gas and the distention had disappeared.

Patient 4

A 50-year-old male underwent a routine right inguinal hernia repair. Two days later, he complained of abdominal distention, slight abdominal discomfort, and inability to pass gas. The abdomen was soft but distended and tympanic on percussion, with no tenderness. Plain x-ray study of the abdomen showed a dilated large bowel. Despite nasogastric suction and mobilization and insertion of a rectal tube, the distention continued for five days before abating.

Patient 5

A 67-year-old man, who had recently been diagnosed as having renal failure, was transferred from another hospital because of a believed intestinal obstruction. He was complaining of abdominal pain and distention, but was unable to pass gas. The patient was in distress but had stable vital signs. His abdomen was distended with slight tenderness throughout, especially in the lower portion. Tympanic sounds were obtained on percussion and bowel sounds were sluggish. Nasogastric suction was started and intravenous fluids administered. His metabolic abnormality was corrected when hemodialysis was started. Over the next few days, his condition improved dramatically: the abdominal pain and distention disappeared and he was able to pass gas.

Discussion

Ogilvie's syndrome is relatively uncommon but not rare. It is also called pseudoobstruction of the large bowel.[1,2] It is defined as acute dilatation of the large bowel without organic obstruction, though the pathophysiology of the syndrome is still obscure. It was first described by Ogilvie[1] in 1948, who suggested the cause to be sympathetic deprivation of the large bowel. In recent studies, however, it has been postulated that it is due to a functional denervation of the sacral parasympathetic nerve supply.[3,4] It is probably sufficient to identify the pathogenesis as an imbalance between the sympathetic and parasympathetic nerve supply of the large bowel.

Extracolonic causes have been implicated in about 90% of the cases. These include heart failure, myxedema, hypokalemia, myocardial infarction, normal pregnancy, postdelivery, fracture of the back, hypotensive agents (ganglion blockers), retroperitoneal hematoma, severe backache, diabetes, anemia, burns, and abdominal radiation.[5-7] In about 10% of the cases, no cause could be identified.[12] In our series, two cases were due to metabolic causes (uremia and hypokalemia), and severe backache, fracture of the spine, and post hernia repair accounted for the remaining three cases.

Patients usually present with a distended abdomen, with or without abdominal pain, and inability to pass gas. Abdominal examination usually reveals slight tenderness throughout, especially in the lower abdomen, tympanic sounds on percussion, and sluggish or absent bowel sounds.[6,13] Plain films of the abdomen typically show a distended large bowel, especially involving the cecum and ascending and transverse colon (Figure 1). Distention of the cecum poses the greatest danger because its thin wall makes it the most vulnerable to rupture, and although rare, this will lead to fatal generalized peritonitis. Therefore, a plain x-ray film of the abdomen should be done daily to determine the diameter of the cecum.

Organic obstruction can only be excluded by sigmoidoscopy, and in cases where no cause can be found, barium enema may be the definitive study. Initially, treatment should be conservative,[4,7] consisting of nasogastric suction, intravenous fluid administration, rectal intubation, and cautious rectal washout with warm saline, along with correction of any electrolyte imbalance and other related causes. This will be successful in most of the cases. The patient must be closely observed and abdominal examination must be a regular part of the regimen. Prostigmin (a parasympathomimetic agent) should not be given, as this may increase the intracolic pressure and lead to perforation.

If conservative treatment fails, colonoscopy should be done. Nanni et al[6] had some reservations concerning the use of colonoscopy to deflate a dilated colon and considered the procedure hazardous. Most other series, however, report very good results from colonoscopy in this disorder, with minimal or no side effects.[8-11] In our series, all five patients were managed conservatively and all recovered well.

For the minority of cases in which colonoscopy is not effective, surgery is called for,[14-16] consisting of colostomy, tube cecostomy, right hemicolectomy, or simply emptying the bowel.

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ATYPICAL PITYRIASIS ROSEA: REPORT OF TWO CASES AND REVIEW OF THE LITERATURE

Mohammed A. Siddiqui, MD

Pityriasis rosea is not the distinctive dermatosis that is commonly depicted in most textbooks of dermatology. Since Gilbert's first accurate description of the disease published in 1860,[1] many new and atypical forms have been described.

The classic form of pityriasis rosea is readily identified clinically. The individual lesions are typically oval or annular with their long axes parallel to the lines of cleavage of the skin. In most cases, the eruptions involve the trunk and are sparse on the extremities, but do not involve the face, neck, hands, and feet. The cases of two patients with pityriasis rosea who manifested palmoplantar lesions are described and the present state of knowledge regarding the clinical presentation and management is summarized.

Case Reports

Patient 1

A 45-year-old physician was seen at the dermatology outpatient clinic 7 days after small scaly pruritic lesions appeared on the lateral side of the right sole and following a mild episode of sore throat.

On examination, the patient was found to have a brownish patch of hyperpigmentation with a narrow erythematous collar. The patch was more firm and keratotic than adjacent skin of the sole and showed peeling at the periphery. Potassium hydroxide preparation for fungus detection was negative. One week later, diffuse erythematous oval lesions appeared on the trunk and upper arms along the cleavage lines of the body. There were fine scales at the periphery. The most striking feature was a few painless brownish, flat papular lesions on the palms and soles with fine superficial scales. The lesions were similar to the initial lesion on the foot, which was the herald plaque (Figure 1).

There was mild cervical lymphadenopathy. The mucous membranes, nails, and scalp were not involved. There was no history of drug intake or genital sores.

Blood count, serological findings, and erythrocyte sedimentation rate were within normal limits. A biopsy specimen from one of the hyperkeratotic lesions showed scattered chronic inflammatory cells in the dermis. The findings indicated a nonspecific dermatitis. The body lesions healed after four weeks, but the lesions on the palms and soles persisted and showed fissuring with peripheral scales. Various local applications were tried, including steroids, but with no success. The patient was then given 30 mg of prednisolone per day by mouth for the first week, 20 mg the second and third weeks, and 10 mg the fourth week, by which time the lesions had healed but postinflammatory hyperpigmentation remained.

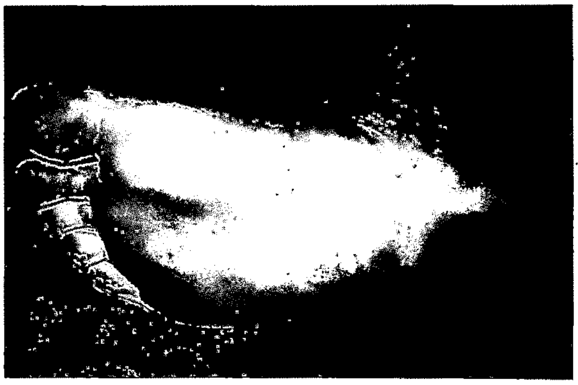

FIGURE 1. The herald patch with smaller lesions.

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Patient 2

A 40-year-old Asian man experienced a localized scaling area on the thenar eminence of the left palm. Two weeks later, smaller lesions appeared on the right palm, neck, upper trunk, and axillae (Figure 2). Most were oval and located along the lines of cleavage. Lesion size ranged from 0.5 to 2.0 cm. Fine scaling was present on the periphery. At about the same time, the patient noted well-defined scaly areas on the soles. The patient had had a sore throat one week prior to the appearance of the palm lesion.

Leukocyte count, erythrocyte sedimentation rate, urinalysis, chest x-ray study, and serological test for syphilis were normal. A skin specimen obtained by punch biopsy showed microscopic changes of chronic dermatitis compatible with pityriasis rosea. Biopsy specimen from the palm showed thickening of the stratum corneum with small areas of mild inflammatory cell infiltrate in the upper dermis.

During four weeks, the skin eruption gradually faded but the palmoplantar lesions remained. Fissuring and scaling were prominent in them. Salicylic acid (5%) was not beneficial, but a short course of steroids given orally (30 mg/day for the first week, 20 mg/day for the second, 15 mg/day for the third) cleared the lesions.

Discussion

Pityriasis rosea, although described in the old literature, was recognized as an entity only in 1860 by Gilbert.[1] Since then, many clinically atypical forms have been noted.

The classic form involves the trunk in a dermatomal pattern, referred to as a Christmas tree distribution. The face,[2] scalp,[3] hands and feet, and mucous membrane[4] are involved less frequently. A localized form of pityriasis rosea in which the lesions are limited to the extremities has been termed *inverted pityriasis rosea*.[5] Pruritus is usually present in pityriasis rosea and recurrences are rare.[6] Morphological variations in the form of vesicular eruption,[7] wheal formation,[8] circinate pattern,[9] and multiform lesions[10] have been described. The vesicular form of pityriasis rosea is more commonly seen in children.

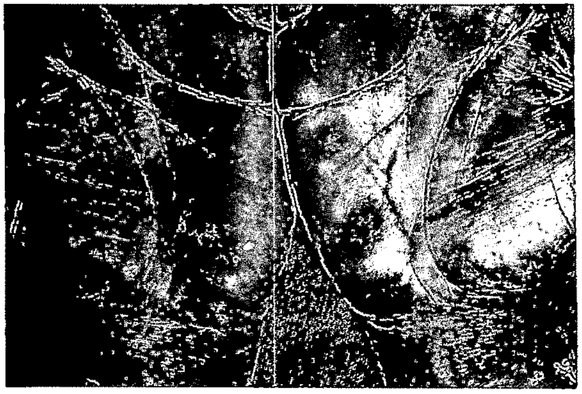

FIGURE 2. The herald patch on the left palm and smaller lesions on the right.

The herald patch, which is usually oval and 2 to 4 cm in length, can be gigantic.[11] It commonly occurs on the trunk but has been known to occur on the face, neck, palms, dorsum of the foot,[6] and penis.[12]

The initial lesion in Patient 1 was unmistakably a herald patch, but this is, to the best of our knowledge, the first report of herald patch on the sole. It was originally presumed that pityriasis rosea does not occur on the hands and feet, but in fact, cases are seen[13] but with less frequency than the cases involving the face and neck. However, the lesions on the palms and soles were rare even in the study by Little. Baily[14] was the first to report palmoplantar lesions of pityriasis rosea. Soles are affected less often than palms.[15] Combes[16] described five forms in which lesions appear on the hands and feet: (1) discrete red plaques, (2) livid red, slightly raised maculopapules with tiny vesicles on the dorsum of hands and feet, (3) scaly red patches on the inner surface of the palms and soles, (4) closely arranged dyshidrotic vesicles, and (5) generalized scaling and redness of the palms and soles. Deep dusky red lesions with a collarette of scales resembling syphilids were also seen.

The etiology of the disease is unknown. There is evidence of infectivity, as indicated by reports of the disease occurring in one household[17] and the presence of prodromal symptoms[18] and of preceding tonsillitis,[19] but the viral and bacterial isolates are not consistent.[20] Decreased duration of illness was observed in a small group of patients following transfusion of serum obtained from convalescing patients.[6] The latest investigations focus attention on autoimmune etiology.[21]

The diagnosis of pityriasis rosea is mainly based on clinical findings. There are no laboratory tests that can confirm it. Prodromal symptoms of malaise and sore throat are irregularly encountered.[18] The tonsils or lymphoid structures of the throat were found to be affected preceding appearance of the skin lesions in 94% of the cases.[19] Blood counts are usually normal, although occasional cases of lymphocytosis and eosinophilia have been reported.[22] A reversal of the albumin/globulin ratio and elevation of the alpha$_2$-globulin content have also been reported.[19]

The course of pityriasis rosea is variable. The usual duration is 5 to 8 weeks, but the lesions on the palms and soles take more time to heal,[10] as evidenced by our observations, and do not respond well to the usual treatment. Because of the unknown etiology, various modalities have been tried on an empirical basis and include tar lotions, sulfur baths, and salicylic acid. Intradermal injection of streptococcal vaccine[23] has been tried, with some benefit. Saline extracts of scrapings from the herald patch injected intradermally have not produced encouraging results.[24] Transfusion of serum from convalescent patients in any form of ultraviolet radiation phototherapy has yielded equivocal results.[6] In the patients reported here, who had palmoplantar lesions, a short-term course of steroids proved to be the most beneficial.

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Editor's Note: Although herald plaques of the palms and soles would be impossible to diagnose at onset, the occurrence of such cases reinforces the old rule not to rush into treatment until the proper diagnosis is made.

HEPATIC INVOLVEMENT IN HEREDITARY HEMORRHAGIC TELANGIECTASIA

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Hereditary hemorrhagic telangiectasia (HHT), or Osler-Weber-Rendu disease, is an autosomal dominant condition characterized by multiple telangiectasia that may involve virtually every organ and marked by recurrent episodes of bleeding.[1] Liver involvement in the presentation of HHT has been rarely encountered.

We report a case of HHT with multiple hepatic telangiectasia that posed problems in treatment. To the best of our knowledge, this is the first such case reported in the English literature.

Case Report

A 32-year-old woman had suffered from HHT since childhood. Her father and sister were also affected. She had been hospitalized several times since childhood because of recurrent epistaxis, melena, and hemoptysis requiring blood transfusion and oral iron supplementation. In September 1985 she began to have paroxysmal episodes of severe pain in the right upper abdominal quadrant that radiated to the right shoulder. These lasted 2 to 3 hours and occurred three to four times a week. The episodes were precipitated by doing housework and were relieved only by narcotic analgesics. There was no history of jaundice or biliary symptoms, and she neither smoked nor drank alcohol.

Physical examination revealed telangiectatic lesions on the lips, tongue, and buccal mucosa. A grade 3/6 systolic murmur was heard over the precordium. The liver was enlarged by 2 cm and was nontender, regular, and firm. No bruit was heard over the hepatic area. There was no ascites, splenomegaly, or the stigmata of chronic liver disease. Other findings from physical examination were unremarkable.

Laboratory findings included the following: hemoglobin, 100.00 g/L; microcytic hypochromic blood picture and low serum iron content with high total iron binding capacity; platelets, 250 × 10^9/L; prothrombin time, 14.5 seconds (control, 13.0); partial thromboplastin time, 39 seconds (control 34); total bilirubin, 12.2 μmol/L (reference interval, 2.6-17.1); alkaline phosphatase, 3.5 μkat/L (reference interval, 0.72-2.57); SGOT, 0.92 μkat/L (reference interval, 0.12-0.67); SGPT, 1.08 μkat/L (reference interval, 0.10-0.88); gamma-glutamyl transferase, 1.43 μkat/L (reference interval, 0.12-53); and serum albumin, 28 g/L (reference interval, 35-50). Serological tests for hepatitis B surface antigen, antimitochondrial antibodies, smooth muscle antibodies, and antinuclear factor were all negative. Fecal occult blood tests were positive on several occasions. Chest radiograph, electrocardiography, and echocardiography were all normal. Upper gastrointestinal tract endoscopy revealed no varices or telangiectasia in the esophagus, stomach, and duodenum. Ultrasonography showed a diffuse hyperechoic pattern of the liver parenchyma and normal intrahepatic biliary tract. The common hepatic artery was enlarged contiguous with dilated tubular structures (Figure 1). The gallbladder and common bile duct were normal. In view of the above sonographic findings, non-contrast-enhanced computed tomography (CT) of the liver was done and revealed multiple hypoat-

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tenuated areas (Figure 2A). After contrast enhancement, these areas became isodense, suggesting vascular abnormalities in the liver parenchyma (Figure 2B). Labeled red blood cell radioisotope liver scan showed irregular distribution of activity with areas of increased vascularity in the right and left lobes. Selective celiac arteriography confirmed the dilated hepatic artery, tortuous intrahepatic arteries, and focal aggregation of contrast medium throughout both lobes of the liver, suggesting vascular malformation in the parenchyma but no hemangioma (Figure 3).

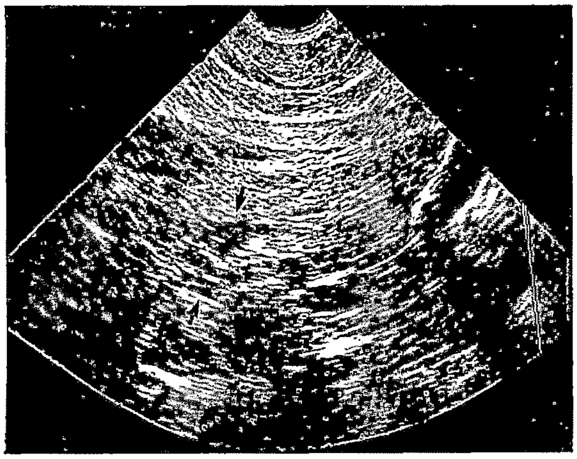

FIGURE 1. Ultrasound examination of liver at porta hepatis revealed multiple vessels (arrows) from collateral circulation.

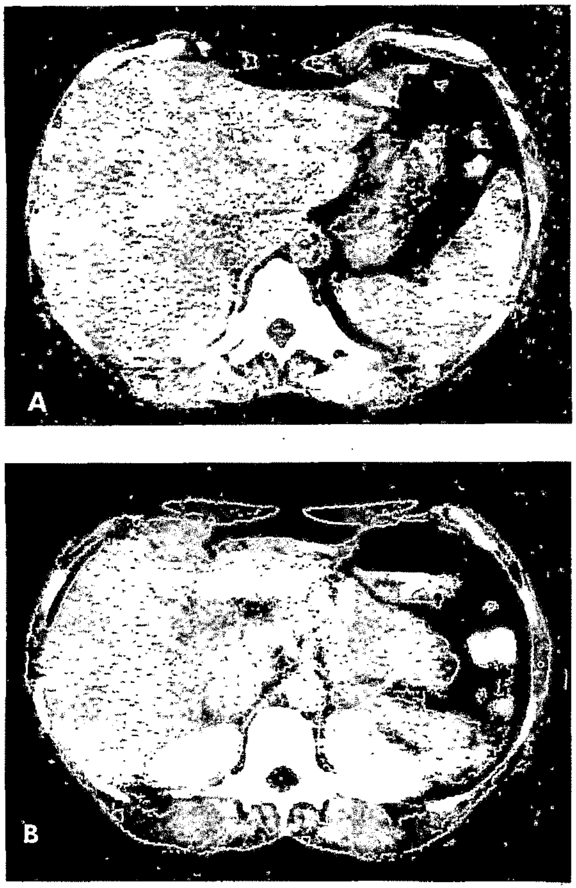

FIGURE 2. (A) Precontrast computed tomographic scan of liver showing multiple hypoattenuated areas. (B) After intravenous contrast injection, hypoattenuated areas became isodense, suggesting diffuse vascular lesion.

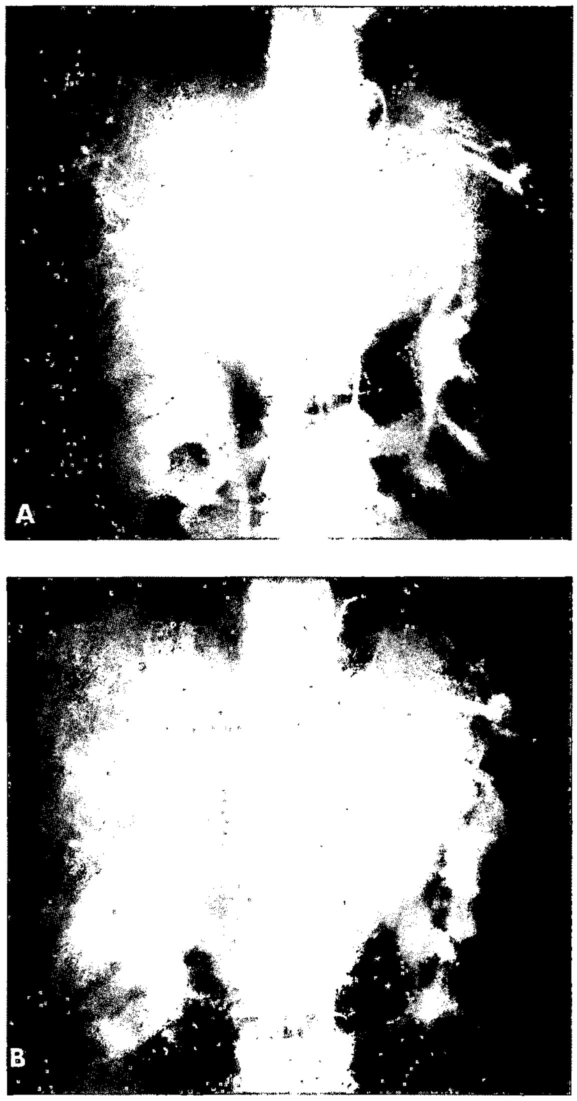

FIGURE 3. (A) Selective celiac axis angiography (early arterial phase) showing tortuous intrahepatic arteries and patchy accumulation of contrast throughout the liver, suggesting vascular malformation. (B) Late hepatic arterial phase revealed nonhomogeneous liver parenchyma due to accumulation of contrast in vascular malformation. There is still contrast in the splenic artery but none in the hepatic artery.

Multiple hepatic telangiectasia was diagnosed, and this was probably the cause of the hepatic bleeding and right upper quadrant abdominal pain. She was started on estrogen, 1.25 mg daily, and ferrous sulfate, 900 mg daily.

By three months, the epistaxis had stopped but the abdominal pain had not abated. Propranolol, 60 mg daily, was then added to the treatment. Six weeks later she noticed marked reduction in the right upper quadrant pain, and she no longer required narcotic analgesia.

During one year of follow-up, while still on treatment, she had one episode of epistaxis but no recurrence of abdominal pain.

Discussion

The specific hepatic pathology associated with HHT has been a subject of considerable controversy. Patients with HHT are at risk of developing liver disease in several ways. These include the direct involvement of liver with HHT in the form of an arteriovenous malformation as well as isolated microscopic telangiectasia in the liver parenchyma and over the smooth shiny capsule. A unique form of focal fibrovascular lesions, called telangiectasia-associated hepatic fibrosis, was also recently reported.[2,3] Chronic anemia and arteriovenous shunt can lead to passive hepatic congestion secondary to high output heart failure. Liver involvement in HHT can also result from the treatment used. Liver damage caused by long-term estrogen therapy can lead to peliosis hepatis, hepatic adenoma, or even hepatocellular carcinoma.[4] Iron overload secondary to repeated transfusion or long-term therapy for recurrent bleeding can cause liver damage, and transfusion-associated acute hepatitis followed by chronic active hepatitis and cirrhosis is also well documented.

The diagnosis of hepatic telangiectasia is usually confirmed by angiography. As seen in our patients, selective celiac axis angiography will show dilated and tortuous intrahepatic arteries, with patchy accumulation of contrast medium in the liver in the early arterial phase suggesting vascular malformation. Her abdominal pain was apparently due to rupture of telangiectasia into the liver. The unusual clinical manifestation of multiple hepatic telangiectasia observed in our patient has not been mentioned in the literature to the best of our knowledge.

The therapy for hemorrhage in HHT, regardless of the source, has been disappointing. Selective proximal ligation of the hepatic artery branches and balloon embolization have been used,[5,6] but because of the disseminated hepatic telangiectasia in our patient, these techniques could not be used. Medical therapy for epistaxis in HHT has included the use of estrogen,[7] which is believed to induce squamous metaplasia of the nasal mucosa, thereby protecting abnormal vessels from minor trauma.[8] Electron microscopic findings have shown that estrogen also re-establishes the continuity of an abnormal vessel.[9] The continuous administration of oral propranolol in a dose that reduced resting heart rate by 25% was shown to produce a sustained decrease in hepatic blood flow in a patient with cirrhosis.[10] Our patient's epistaxis stopped after treatment with estrogen, but the frequency and severity of abdominal pain eased only upon the addition of propranolol to her regimen. This reduction in abdominal pain could be due to the estrogen, through re-establishment of the endothelium of abnormal liver vessels, or due to decreased hepatic telangiectatic vessels.[9,10]

We recommend the additional use of propranolol if estrogen alone is not effective in relieving symptoms.

Acknowledgment

We thank Marilu Velarde for typing this manuscript.

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Letters to the Editor

The *Annals of Saudi Medicine* welcomes letters to the Editor from its readers. They may be on any topic, though the Editor especially encourages discussion of papers published in the *Annals*. Letters should be no more than 100 typewritten lines in length, typed double-spaced, and submitted in triplicate. Letters may include one figure or brief table and up to five references. Submission of a letter constitutes permission for the *Annals* to use it for publication, and letters should not duplicate similar material being submitted or published elsewhere, and the *Annals* reserves the right to edit letters submitted. Letters referring to a recent *Annals* article should be received within 6 weeks of the article's publication.

Adolescent Pregnancy and Perinatal Outcome

To the Editor: I read with interest the paper by Ba'aqeel[1] and agree with the author's conclusion that the different social and behavioral conditions in Saudi society, where marriage and pregnancy are common among teenage girls, are more important determinants of outcome in adolescent pregnancy than the young age of the mother per se. Nonetheless, his data do show that there was a significant difference between adolescent mothers, aged 15 years and younger, and the control group with regard to fetal weight and size. The risk of adverse fetal outcome in teenage mothers in the Arab population can be illustrated from our experience in Benghazi.[2]

The cases of 16,365 consecutively live-born neonates born over a period of 12 months were studied prospectively for evidence of birth asphyxia, that is, if infants required intermittent positive pressure ventilation (IPPV) for more than a minute before sustained respiration occurred or had an Apgar score of less than 5 at 1 minutes. If IPPV was administered for 3 minutes, this was indicative of severe birth asphyxia.

We found that asphyxia occurred in 2.8% of all live-born neonates. Multivariate analysis of high-risk factors associated with increased risk of asphyxia showed that low birth weight was the most significant predictor: asphyxia occurred in 68% of infants with a birth weight of less than 1,000 g and in 1.2% of infants with a birth weight of 3,000 to 4,000 g. Other perinatal risk factors associated with a higher incidence of asphyxia include postmaturity and birth weight greater than 5,000 g accompanied by maternal and/or obstetric complications. The relationship of maternal age and parity to the incidence of birth asphyxia is shown in Table 1. Although more primiparas delivered asphyxiated live-born neonates than did multiparas, the difference between the two groups was not significant *($P > 0.05$)*. However, a maternal age of 15 years or younger was associated with a greater than fivefold increase in the incidence of birth asphyxia.

The different social, behavioral, and educational status of women in urban areas of Saudi Arabia such as Riyadh may result in improved perinatal statistics. However, improvement in perinatal outcome may not be witnessed in rural areas where a woman's passage to adulthood is determined by menarche and physical development, without consideration for the woman's emotional and educational development.

In some underdeveloped areas of the world, marriage before puberty is not uncommon, and a five- to seven-fold increase in the perinatal mortality is seen among mothers 15 years and younger.[3] With economic improvements paralleling better health-care delivery, Japan has seen a dramatic decline in perinatal mortality. One of the major contributing factors to this improved perinatal outcome has been the introduction of pre-pregnancy maternal and child health medical education and guidance services.[4] In another

TABLE 1. *Maternal age and parity and incidence of birth asphyxia.*

Variables	Incidence	*P* value
Parity		
Primipara	110/1955 (5.6%)	NS
Multipara	355/14,410 (2.4%)	NS
Maternal age		
≤15	2/13 (15.4%)	<0.001
16–20	75/2390 (3.1%)	NS
21–30	250/10,340 (2.4%)	NS
31–40	135/3499 (3.8%)	NS
≥41	3/123 (2.4%)	NS

NS = not significant.

study, improving the delivery of prenatal care in adolescent mothers was shown to have a positive effect on birth weight and duration of gestation.[5]

The lack of adequate socioeducational knowledge and emotional development in adolescent mothers is itself a risk factor and more attention must be given to the care of the at-risk mother, fetus, and newborn.

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Reply

To the Editor: I thank Professor Mir for his comments concerning my manuscript on young maternal age and perinatal outcome. The main point raised by Professor Mir is that teenage pregnancy does not necessarily have a favorable outcome, especially when compounded by suboptimal social, economic, and educational conditions, as are found in rural areas. This is an established fact. However, what are the factors that predispose to an unfavorable outcome in these young mothers? Is it biological age per se or other factors such as parity, medical complications, social habits, availability of health care, and nutritional status? In my study, most of the above factors were controlled for through an historical prospective design so that the effect of age could be examined in some isolation. The results indicate that young maternal age per se is not associated with poor outcome. This is corroborated by other recent findings, as detailed in my article. Therefore pregnancy in a teenager does not automatically represent a high risk. When faced with a pregnant teenager, perinatal care providers should look for other confounding factors such as malnutrition, medical/obstetric complications, and compliance in attending antenatal clinics, before categorizing her as a high risk on the basis of age alone.

Professor Mir indicates that they examined risk factors for birth asphyxia. Multivariate analysis showed that low birth weight, postmaturity, macrosomia, and presence of medical and/or obstetric complications are associated with birth asphyxia. The reported relationship between young age and birth asphyxia shown in the Table indicates that birth asphyxia occurred in 5.6% of the deliveries in primiparas versus 2.4% in multiparas, and this was reported as nonsignificant. My calculations show that this is a highly significant difference ($P < 0.0001$)! The table data seem to be uncontrolled for factors that are known to predispose to birth asphyxia. The fivefold increase in birth asphyxia in mothers 15 years of age or younger cannot be attributed to young maternal age alone when there are no data given concerning the other factors. It is also not clear from Professor Mir's letter whether his multivariate analysis of risk factors retained young age as an independent risk factor for birth asphyxia.

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A Case of Ileoileal Neonatal Intussusception

To the Editor: Intussusception in children is a common abdominal emergency that occurs most commonly in infants during the fifth to ninth month.[1] However, intussusception in the newborn is rare,[2] and in contrast to classic intussusception, the clinical features are difficult to recognize, leading to delayed diagnosis and increased morbidity and mortality. We report a case of ileoileal intussusception in a newborn due to an intestinal polyp.

A premature (gestation, 36 weeks; birth weight, 2460 g) female infant was the product of a normal vaginal delivery. The infant had an Apgar score of 9 and 10 at 1 and 5 minutes, respectively, and examination findings were normal. She passed normal meconium at 12 hours, but at 24 hours abdominal distention and bile-stained vomiting started to develop. She was not given any feedings, and examination showed a distended abdomen, visible peristalsis with increased bowel sounds, and palpable loops of intestine. There was no tenderness or masses. Rectal examination revealed heavily blood-stained meconium. Erect and supine x-ray studies of the abdomen showed dilated loops of small bowel with multiple fluid levels. The diagnosis of volvulus could not be excluded and exploration laparotomy was advised, but the parents refused and took the infant home against medical advice. Five days later, the patient was readmitted to the hospital in a toxic and severely dehydrated condition. Examination at this time revealed marked abdominal distention, tenderness, and absent bowel sounds. No masses could be felt. Erect and supine x-ray films of the abdomen showed gross dilatation of the intestine with multiple fluid levels. After resuscitation, emergency exploratory laparotomy was performed which revealed dilated loops of small intestine and ileoileal intussusception with necrosis and perforation. This was reduced partially, and resection of 27 cm of small intestine (Figure 1) with an end-to-end anastomosis was done. Histological examination of the resected specimen showed transmural necrosis with perforation of the intestine; a polyp was found which was the likely cause of the intussusception. Postoperatively, the patient made a good recovery and was discharged home well.

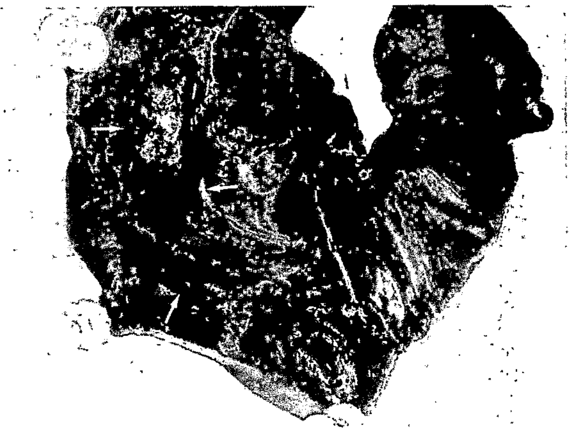

FIGURE 1. Specimen removed at operation, showing the intussusception.

Neonatal intussusception is rare and its clinical features differ from those of classic idiopathic intussusception, making diagnosis difficult, and thus increasing the morbidity and mortality.[2] Usually intestinal obstruction is the presenting sign, often occurring within the first day of life.[3] A high index of suspicion for neonatal intussusception is necessary to avoid the reported 57% incidence of bowel gangrene or perforation at the time of surgery.[3] Patriquin et al,[3] in a review of 25 cases and 12 of their own, outlined the frequency of the clinical signs and symptoms of neonatal intussusception. They reported abdominal masses in only 24% of their cases of neonatal intussusception, while reports of classic idiopathic intussusception[4-6] cite a 50 to 74% incidence of abdominal masses. The lower figure for neonatal intussusception may be related to the high frequency of abdominal distention in such cases (65%),[3] which makes it difficult to feel the mass. In classic intussusception abdominal distention has been found in only 9 to 17% of cases.[4,5] Necrotizing enterocolitis and small bowel volvulus must be considered in the differential diagnosis, but diagnosis is made easier when a mass is palpable.

Typically, intussusception does not involve a precipitating cause, and such events occur in children who are older than 2 years.[6] In neonatal intussusception, a precipitating cause (e.g., duplication cyst, Meckel's diverticulum, polyp) is present in over 32% of cases,[3] so no special efforts should be made to manage the disorder except by surgical means.

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Symposium Abstracts

THIRD SYMPOSIUM ON GASTROENTEROLOGY AND HEPATOLOGY

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NATURAL HISTORY OF CHRONIC VIRAL HEPATITIS B, GL Davis, University of Florida, Gainsville, Florida, U.S.A.

Although hepatitis B virus infection is a major worldwide health problem, it is far less common in the U.S. and is confined largely to persons in specific high-risk groups, such as Asian immigrants, homosexual males, intravenous drug abusers, dialysis patients, multiply-transfused patients (e.g. hemophiliacs), and medical personnel. The likelihood of developing chronic infection is only 5 to 10%, far less than in non-A, non-B hepatitis. However, the risk of chronicity is higher in certain subgroups, including neonates, children, dialysis patients, and immunosuppressed individuals. It is estimated that chronic type B hepatitis affects at least one million individuals in the U.S. Chronic type B hepatitis has two phases of infection: the early replicative phase during which disease is virologically (HBeAg & HBV-DNA+), biochemically (increase ALT), and histologically active, and the later nonreplicative phase which occurs after HBeAg seroconversion and is characterized by histologically inactive disease, anti-HBe positivity, and usually normal liver tests. The replicative phase of infection is clinically most important and represents the period when risk of progressive liver disease occurs. Approximately 25% of patients develop cirrhosis within 5 years. Ten to 15% of patients will undergo HBeAg seroconversion and enter the nonreplicative phase of infection each year, although up to 30% may experience transient reactivation of disease (return to the replicative phase). Despite this natural "burning out" of the infection, morbidity and mortality of this disease is high. The overall 5-year survival of HBsAg-positive patients is 70% (50% in cirrhotic patients), and 40% of all carriers will die of their liver disease.

TRANSMISSION OF HEPATITIS B, FZ Al-Faleh, College of Medicine, King Saud University, Riyadh

The question of transmission of hepatitis B has been a major issue in many studies and the topic of several symposia worldwide. Several studies in Saudi Arabia have studied the transmission of hepatitis B infection. This presentation will review and update the different aspects of hepatitis B transmission, with special reference to Saudi Arabia.

NON-A, NON-B HEPATITIS: AGENTS, DISEASE, DIAGNOSIS, AND PREVENTION, MS Khuroo, Armed Forces Hospital, Riyadh

Non-A, Non-B hepatitis (NANBH) is caused by a group of putative viral agents which have not been identified or characterized. There are two types of NANBH, namely, transfusion-associated NANBH (TNANBH) and epidemic NANBH (ENANBH). TNANBH is presumed to have at least two etiologic agents, namely long-incubation TNANBH and short-incubation TNANBH. TNANBH was first recognized in patients with blood-transfusion-associated hepatitis in Western Europe, the U.S., and Japan. The disease is also prevalent in persons receiving blood products (factor VIII and factor IX therapy), those exposed to needle pricks (staff and patients of hemodialysis units), and illicit intravenous drug users. Long-incubation TNANBH has an incubation period of 7 to 10 weeks, occurs following factor IX therapy, and has a chronicity rate of 10%. Short-incubation TNANBH has an incubation period of 1 to 3 weeks, occurs following factor VIII therapy, has fluctuating enzyme elevations, and a chronicity of 50 to 90%. The disease leads to a high incidence of chronic hepatitis and cirrhosis. Recently, cases of hepatocellular carcinoma in patients with TNANBH have been recorded from Japan. TNANBH has been transmitted to a host of experimental animals, including chimpanzees. However, its serologic tests are claimed to diagnose TNANBH. All these tests lack specificity, reproducibility, and confirmability by independent laboratories. ENANBH was for the first time recognized during an epidemic which occurred in the Kashmir valley in 1978. Soon, it was evident that all water-borne or water-related epidemics of hepatitis in the adult population of India and many other developing countries are related to ENANBH. ENANBH presents a national health problem in India. There is convincing epidemiologic evidence that ENANBH is a water-borne disease. ENANBH has, in the icteric form, increased incidence and severity in pregnant women and this is one of the most characteristic epidemiologic features of the disease. The transaminase rise is modest and monophasic. The disease is self limiting with eventual clinical recovery in non-fatal cases. The major agent of human ENANBH appears to be a virus-like particle that is approximately 27 nm in diameter and that sediments in sucrose gradients at 183S. The data strongly suggest that one virus is responsible for most cases of ENANBH observed worldwide. ENANBH is the most common cause of sporadic acute viral hepatitis in developing countries. NANBH causes 4.3 to 25% of acute sporadic hepatitis in Western Europe and the U.S. ENANBH can occur as a superinfection in patients with hepatitis B carrier state and present as an episode of acute viral hepatitis superficially resembling acute hepatitis B. The diagnosis of ENANBH during epidemic hepatitis does not cause diagnostic problems. Diagnosis of sporadic NANBH needs exclusion of acute markers of hepatitis viruses; exposure to hepatotoxin and hepatotoxic drugs; systemic disease likely to cause hepatic damage. Confirmation of diagnosis of NANBH in chronic hepatitis of unknown cause and cryptogenic cirrhosis must await serologic tests for NANBH. Recent data show that low-dose interferon therapy may be useful in chronic TNANBH. As ENANBH is an ecologically determined disease, its control would depend on improved sanitation, proper sewage disposal, and a supply of safe portable water. The use of immune serum globulin has considerably reduced mortality when used in third-trimester pregnant women in one outbreak in Kashmir. Blood banks use voluntary blood to reduce the occurrence of TNANBH. Exclusion of donors with elevated alanine transferase partially reduced the transfusion-associated hepatitis. Anti-HBc could be used as a secondary screening procedure for TNANBH. Last, use of immune serum globulin reduces the frequency of transfusion-associated hepatitis and its progression to chronic active hepatitis.

PREVENTION OF HEPATITIS B VIRUS INFECTION, B Ayoola, King Khalid University Hospital, Riyadh

Hepatitis B virus (HBV) infection poses a global health problem. It is estimated that 300 million people are chronic HBV carriers. Most are located in the developing world where infections occur perinatally or early in childhood. The sequelae of such infections include liver cirrhosis and hepatocellular carcinoma. Both are highly prevalent, and the latter has a rapidly fatal course in middle-aged persons. Preventive strategies have included (1) health education, (2) public health measures such as blood transfusion regulations, (3) passive immunoprophylaxis, and (4) active immunization. Because of several factors, including the fact that the mode of transmission in the majority is unknown and occurs either vertically (mother-child) or horizontally (close contacts) and the fact that other strategies involve long-term commitment of resources, active immunization is considered the most effective and cost beneficial strategy against HBV infections. Several vaccines are now available. There is a plasma-derived vaccine or one produced by DNA recombinant technology. These are safe, immunopenic, and efficacious, and can be given simultaneously with another extended program of immunization (EPI). The World Health Organization (WHO) and other health authorities have rightly recommended the integration of HB vaccine into the current EPI. Some countries are not at the dawn of such strategic commitments. The main constraint is the relatively high cost of these vaccines. Fortunately, the cost of most of them has been reduced by over 800%. Considering the socioeconomic status and large susceptible populations of most developing countries, prices must still be reduced. There are some outstanding issues in the HB vaccinology (e.g., the need for booster vaccination), which only continuing experience in mass immunization projects may resolve. It is believed that global HB vaccination will reduce the reservoir of HBV, the prevalence and incidence of chronic liver diseases, and hepatocellular carcinoma.

HEPATIC FAILURE, DH Van Thiel, School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, U.S.A.

The case fatality rate for various types of hepatitis virus are as follows: 0.14% for hepatitis A, 1% for hepatitis B, and 2.3% for non-A, non-B hepatitis. Liver size initially is normal but decreases rapidly and is followed by ascites. The prothrombin time is the most useful laboratory test for assessing the severity of liver dysfunction in such cases, and yields the most important prognostic information. Levels greater than 5 s above control are worrisome. The serum levels of bilirubin and transaminases vary greatly in fulminant hepatic failure and are not particularly useful as prognostic measures. The striking morphologic features of fulminant hepatic failure due to viral infection are a panlobular destruction of hepatocytes with collapse of the reticulum network, as well as a variable mixed inflammatory infiltrate in the portal areas. Fortunately, the regenerative capacity of the liver is considerable, and in patients surviving fulminant hepatic failure, both liver function and morphology typically return to normal. Occasionally, cases of fulminant hepatic failure are attributed to other more unusual viral infections of the liver such as cytomegalovirus, Epstein-Barr virus, the herpes simplex virus, and various adenoviruses. The principal goals in the clinical management of cases of fulminant hepatic failure are the recognition and early treatment of hepatic encephalopathy and the prevention of hypoglycemia. Cerebral edema should be carefully sought out and monitored. Ideally this is accomplished with the insertion of an extradural central nervous system pressure monitoring device. Mannitol (20%) is the most effective drug for the treatment of cerebral edema due to viral hepatitis. It is administered as a rapid intravenous bolus of 100 ml which can be repeated hourly if necessary. Acute hyperventilation is also of value in such cases but can only be utilized for short periods. When it is not possible to use mannitol because of renal failure, ultrafiltration is a reasonable alternative therapy in cases of fulminant hepatitis failure with cerebral edema. Renal failure occurs commonly in cases with fulminant viral liver disease, and characteristically there is a marked disparity between the blood urea value and the serum creatinine level as a result of the reduced urea synthesis associated with hepatic failure. In all cases with developing renal dysfunction, hypovolemia should be corrected. Dopamine administration at a dose of 2 to 4 μg/kg per hour can be utilized to increase renal blood flow when urine output is adequate. In most cases with overt renal failure, hemodialysis is usually required. The development of renal failure and a metabolic acidosis, however, has a very poor prognosis in individuals with fulminant hepatic failure. An increased susceptibility to infection is also common in fulminant viral hepatitis. This finding is attributed to defective Kupffer cell function and a deficiency of opsonins. Frequent cultures of blood, urine, sputum, ascites, and wound sites should be obtained in all such cases.

PATHOPHYSIOLOGY OF PORTAL HYPERTENSION, V Siva, Security Forces Hospital, Riyadh

Classically, portal hypertension is considered secondary to increased resistance to portal venous flow, but recent experimental studies have suggested that the pathophysiology is much more complex and an increased portal venous flow secondary to splanchnic arteriolar vasodilation plays an important role in the increased portal pressure. Mild, moderate, and severe portal hypertension shows a graded sequence in the pathophysiological changes, and any theory should also explain why ascites is rare in pure presinusoidal portal hypertension, although it may complicate in the terminal stages. Contrary to the traditional view, current evidence points to the fact that ascites is a consequence and not the cause of salt and water retention; it is also interesting to note that under experimental conditions, when a cellophane bag was placed covering the liver in the presence of severe portal hypertension, the fluid collected only inside the bag and nowhere else. The evolution of the hepatorenal syndrome, better known as functional renal failure, is also well understood under the same setting, and some therapeutic approaches soon become clear in the prevention as well as the management of some of these complications.

HEMODYNAMICS OF PORTAL HYPERTENSION, AA Salam, Emory University Hospital, Atlanta, Georgia, U.S.A.

A thorough understanding of the hemodynamics of portal hypertension is essential for the proper management of patients suffering from this disease. With modern diagnostic techniques, one can readily distinguish between the three major categories of portal hypertension, i.e., prehepatic, intrahepatic, and posthepatic hypertension.

GASTROINTESTINAL TRACT INVOLVEMENT IN BRUCELLOSIS, AK Al-Aska, College of Medicine, King Saud University, Riyadh

The clinical presentations of brucellosis are diverse. We studied 340 patients with brucellosis. Gastrointestinal symptoms were anorexia (40%), abdominal pain (16%), vomiting (11%), diarrhea (6%), and constipation (4%). The prominent gastrointestinal tract signs were hepatomegaly (20%), splenomegaly (18%), and hepatosplenomegaly (29%). Liver function tests were abnormal in 14%. Liver biopsy examination showed that, in addition to noncaseating epithelial granulomas, there were nonspecific reactive changes.

PREVALENCE OF HEPATITIS B VIRUS INFECTION AMONG PREGNANT BAHRAINI WOMEN, NR Zayyani, The Arabian Gulf University, Manama, Bahrain

More than 200 million individuals worldwide are infected with hepatitis B virus (HBV). Moreover, perinatal transmission of HBV from infected mother to neonate has been shown to occur at a high rate, often leading to chronic infection of the baby. This study was conducted to determine the prevalence of HBV infection among pregnant Bahraini mothers attending prenatal clinics. The serum from 436 mothers was examined for hepatitis B surface antigen (HBsAg) using enzyme immunoassay (Auszyme; Abbott). Seven asymptomatic mothers were found to be HBsAg positive, for a total carrier rate of 1.6%. Similar rates were reported from Saudi Arabia (1.6-2.3%). Though the prevalence is not as high as in some countries in Southeast Asia (20%), it is much higher than that in the U.S. (0.2%). Prenatal screening and vaccination of babies born to infected mothers are strongly recommended.

ANTI-DELTA AND HBeAg IN HEPATITIS B SURFACE ANTIGEN-POSITIVE INDIVIDUALS, MAF El-Hazmi, College of Medicine, King Saud University, Riyadh

In 1977, "delta antigen" was first discovered by Rizetto and coworkers [Immunofluorescence detection of new antigen-antibody system (delta/anti-delta) associated to hepatitis B virus in liver and in serum HBsAg carriers. Gut 1977;18:997-1003] in the hepatocyte nuclei of Italian HBsAg carriers and recognized as a marker for an infectious agent called the "delta agent." The "delta agent" was found to be expressed only in the liver and was found circulating in the blood of HBsAg carriers. The presence of delta infection was reported to be associated with a high rate of acute mortality and chronic morbidity in patients with hepatitis B virus (HBV) infection. In Saudi Arabia, delta infection in HBsAg carriers was reported to be highly prevalent in several regions of the country, suggesting that Saudi Arabia is an independent foci for delta agent, and a strong association between the delta agent and liver diseases was "identified." To assess the role of delta agent during the infectivity period of HBV infection, we investigated the prevalence of delta antigen in patients with HBeAg and HBsAg positivity. Conversely, we compared the liver function tests in HBsAg-positive patients grouped according to whether they were HBeAg or delta antigen positive, or both, and the influence of both antigens on the morbidity in HBeAg carriers was investigated. The results showed several liver function test abnormalities and a significantly higher morbidity associated with the coexistence of the HBeAg and delta antigen in HBsAg-positive carriers.

DIAGNOSTIC ROLE OF ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION IN DIAGNOSIS OF INTRA-ABDOMINAL MASSES, IA Al-Mofleh, RS Al-Rashed, H Raber, FH Shipkey, College of Medicine, King Saud University, Riyadh

Recently ultrasound-guided fine needle aspiration (US-FNA) has been found to improve the diagnostic yield of abdominal masses and has decreased the need for exploratory laparotomy. Over the last 18 months, we performed 141 procedures on 134 patients (five patients had aspiration from multiple organs and in two patients the procedure was repeated). Patients were sent from different clinics and wards for US-FNA after their abdominal ultrasound examination revealed one or more lesions. Patients were accepted for US-FNA after assessment of US films and exclusion of severe coagulation disorder. All patients received 2 mg of lorazepam orally one hour prior to the procedures. The fine-needle gauge ranged from 20 to 23. After skin disinfection, local anesthesia was applied at the site selected by US. Most patients were Saudi and Yemeni: 63 and 22%, respectively. The youngest patient was 16 and the oldest 82 years old. Males comprised 63% of patients. The most common presenting symptoms were abdominal pain, abdominal mass, weight loss, fever, and jaundice in 41, 27, 24, 14, and 13% of patients, respectively. No complications were encountered. We conclude that US-FNA was accurate in diagnosing intraabdominal masses. Aspirate from focal lesions of the liver was the most common and had the highest yield. In addition, US-FNA was safe; therefore, we recommend its application in the initial diagnostic approach of intraabdominal masses.

Tc-99m SCINTIGRAPHY IN THE DIAGNOSIS OF HEPATIC HEMANGIOMA, M El-Desouki, IA Al-Mofleh, RS Al-Rashed, RS Al-Hmaid, King Khalid University Hospital, Riyadh

Hemangiomas are the most common benign tumor of the liver. Differentiating hemangiomas from other hepatic lesions is important, not only for proper management of the patients, but also to avoid the risk of needle biopsy. To determine the role and accuracy of Tc-99m RBC scintigraphy in establishing the diagnosis of hepatic hemangiomas, 24 patients with different focal hepatic lesions were investigated. The final diagnoses were hemangioma (14 patients), hepatomas (three), metastasis (three), and cyst, abscess, hematomas, and regenerating nodule (one each). The diagnoses were made by angiography, surgical exploration, biopsy, fine-needle aspiration, or clinical stability for 9 to 22 months. Tc-99m RBC scintigraphy, including flow study, and early and delayed (1-2 hrs) blood pool images were performed in all patients. Of the 14 patients with hemangiomas, 13 showed increased blood pool activity over time "reversible blood pool." One hemangioma less than 2 cm in size was not detected. None of the nonhemangioma lesions demonstrated increased blood pool activity in the delayed images. We conclude that Tc-99m RBC scintigraphy is a simple, noninvasive technique that can establish the diagnosis of hepatic hemangioma with a high degree of accuracy.

ASPIRATION CYTOLOGY OF HEPATIC MASSES, MA Ali, M Akhtar, A Burgess, King Faisal Specialist Hospital and Research Centre, Riyadh

Fine-needle aspiration is widely used in establishing a cytological diagnosis. There have been several recent reports on fine-needle aspiration biopsy of liver tumors. At King Faisal Specialist Hospital and Research Centre, between 1977 to 1988, we performed 541 fine-needle aspiration biopsies on liver masses in 463 patients. In 333 (72%) patients, the diagnosis of malignant neoplasm was rendered. Of these, 212 (63.7%) were primaries in the liver and 121 (36.1%) were metastatic neoplasms. In 38 (8%) patients, the diagnosis of benign disease was rendered. In 17 (4%) patients, the results of aspiration biopsy were considered inconclusive. Cytologically, primary hepatocellular carcinoma is diagnosed in aspiration smears by the presence of: (1) clean background, (2) increased nuclear/cytoplasmic ratio and prominent nucleoli, and (3) presence of large numbers of naked nuclei. Metastatic carcinoma usually shows a necrotic background and relatively tight clusters of neoplastic cells. The presence of intracytoplasmic bile, intracytoplasmic eosinophilic inclusion, and fat vacuoles are additional features helpful in differentiating primary hepatocellular carcinoma from metastatic neoplasms. Benign lesions, such as regenerative nodules of hepatic cirrhosis, show well-preserved cell borders, irregular cell clusters, and increased binucleation in the liver cells.

ROLE OF ANGIOGRAPHY IN PORTAL HYPERTENSION, AH Ismaeil, Riyadh Central Hospital

The clinical challenge presented by problems associated with the pathophysiology of hemodynamics of portal hypertension has found no satisfactory solution. Fifty-four patients with portal hypertension underwent angiographic studies, including percutaneous splenoportography, arterial portography, and percutaneous transhepatic splenoportography and left venography, to study the hemodynamics of their portal circulation. The relative merits of each modality and the results were discussed. The postoperative evaluation of the shunt surgery was also emphasized.

HEPATIC GRANULOMA IN AN ARAB POPULATION, B Ayoola, MA Hafeez, RS Al-Rashed, IA Al-Mofleh, College of Medicine, King Saud University, Riyadh

Hepatic granulomas have been the subject of extensive reviews. The relative incidence and etiologic factors vary with different geographic locations. Between 1403 and 1408H (a 6-year period), 788 liver biopsy specimens were obtained for pathologic examination at King Khalid University Hospital, Riyadh. The records of patients with pathologic diagnosis of hepatic granuloma were carefully reviewed. A total of 59 patients (7.5%) had granulomas. Of these, only 44 (32 males, 12 females) had adequate clinical data for further analysis. There were 21 Saudis, 13 Yemeni, and four other nationalities, and ages ranged from 18 to 65 years. Splenomegaly (17), weight loss (16), hepatomegaly (13), and fever (11) were the most common clinical features. Hepatic schistosomiasis was the cause in 21 cases, including four patients with additional etiologic factor viz brucellosis (one), tuberculosis (two), and sarcoidosis (two). In five patients, tuberculosis was the final diagnosis. In four patients the causes included sarcoidosis (one), kal-azar (two), and brucellosis (one). In the remaining ten patients (23%), exact causes were unknown. This is consistent with previous observations that 13 to 36% of granulomas have no known etiology. Despite the limitation inherent in a retrospective study, it may be concluded that the 7.5% frequency is comparable to previous observations of 10%, and that hepatic granulomas are relatively common in Saudi Arabia. Although schistosomiasis is the most common cause, additional factors (e.g., tuberculosis) should be sought in patients from areas of high endemicity for these diseases. The role of drugs especially in the category of granuloma of unknown cause could not be defined in the present study. Larger prospective studies are indicated to define further this clinicopathologic entity in Saudi Arabia.

HEPATOTOXICITY OF ANTITUBERCULAR DRUGS IN SAUDI ARABIA, L Pandya, N Al-Sharif, A Marie, M Kamal, A Madani, Sahary Chest Hospital, Riyadh

Tuberculosis is one of the important infectious diseases prevalent in the Kingdom. Ninety-three percent of the pulmonary tuberculosis patients in Sahary Chest Hospital, Riyadh, receiving first-line antitubercular drugs consisting of streptomycin or ethambutol, INH, rifampicin, and pyrazinamide. The last three drugs are known to be hepatotoxic. Of 838 patients receiving these drugs, 18 patients (2.2%) showed evidence of jaundice during 1407 to 1408H. Of 383 Saudi patients, 17 developed jaundice (4.4%). Only one non-Saudi patient of 455 (0.2%) developed jaundice. Four Saudi patients died (25%); compared to other patients without jaundice the mortality was only 3.2%. Among Saudis, ten patients were males and seven patients females. The average time of onset of jaundice was 16 days from the start of therapy. Eight patients had miliary tuberculosis, one had pleural effusion, and the rest had bilateral extensive lesions. Bilirubin level ranged from 1.4 to 12.4 mg and SGOT from 17 to 100 (normal, up to 18). All antitubercular drugs were stopped in five Saudi patients, while in 12 patients, rifampicin and pyrazinamide were stopped. These 12 patients had continuous INH; bilirubin started going down in all patients. Various factors causing jaundice in Saudi patients may be advanced age, miliary and extensive tuberculosis, prior hepatic damage, genetic variation in metabolizing INH, and malnutrition. The most significant prognostic factor was low albumin, which ranged from 12.0 to 29.0 g/L (reference interval, 35.0 to 50 g/L).

SPONTANEOUS BACTERIAL PERITONITIS (SBP): A REVIEW OF EIGHT CASES, S Barlas, FI Khawaja, King Fahad Hospital, Medina

SBP is an increasingly recognized complication seen in patients with advanced liver cirrhosis and ascites. The clinical features and laboratory data of eight cases of SBP during a 3-year period from 1406-1408 were retrospectively analyzed. There were seven Saudis (87.5%). Male to female ratio was 7:1. Age ranged from 35 to 65 years (average, 47.3). Four patients (50%) were positive for HBsAg. All patients had advanced cirrhosis with ascites, prolonged prothrombin time, and reversed A/G ratio. On ultrasonography, the liver was small and shrunken in two, splenomegaly in five, and ascites in seven. On admission, fever was present in four (50%); encephalopathy, four (50%); increasing ascites with abdominal pain, three (37.5%); UGI bleeding, one (12.5%); hypotension, one (12.5%); and loose motions, one (12.5%). None of the patients had obvious signs of peritonitis. Peripheral WBC count was elevated only in one (12,000/mm^3) and ranged from 3200 to 10,000/mm^3. Admission serum bilirubin averaged 3.67 mg/dl (1.3 to 13 mg/dl); SGOT, 116 U/I (29-180 U/L); SGPT, 95 U/L (22-323 U/I); serum albumin, 2.5 g/dL (1.8-4 g/dL); serum globulin, 4.5 g/dL (1.7-6 g/dL). The ascitic fluid was turbid in six (75%) and clear in two (25%). The ascitic fluid WBC count ranged from 640-12,000/mm^3 and absolute polymorphonuclear count 512-10,200/mm^3 (average, 2620/mm^3). Ascitic fluid protein in all cases was less than 3 g/dl. On microscopy, gram-negative rods were seen in one specimen only. Positive cultures of the ascitic fluid were obtained in five (62.5%). *Klebsiella pneumoniae* isolated in two, *Strep. viridans* one, *E. coli* one, *Acinetobacter calcoaceticus* one. One patient (12.5%) had two episodes of peritonitis 3 months apart with two different organisms. It was *Klebsiella pneumoniae* in the first and *Serratia marcescens* in the second episode. Blood cultures were obtained in all patients. Organisms were grown in 5%. In three patients, the same organism was recovered from the blood and ascitic fluid. In the two with positive blood cultures, the ascitic fluid was negative. The organisms grown from ascitic fluid and blood were sensitive to aminoglycosides, third generation cephalosporins, and pipericillin. Six patients died during the same hospitalization (mortality, 75%). Massive UGI bleeding was the terminal event in three. Four developed hepatorenal syndrome. SBP is not an uncommon terminal event in patients with advanced liver cirrhosis and ascites. All cases of liver cirrhosis admitted with decompensation should have prompt paracentesis. An ascitic fluid polymorphonucleocytosis of over 250 cells/mm^3 establishes the diagnosis. With increasing awareness, more patients might be salvaged with prompt and aggressive therapy.

LIVER ABSCESS IN KING KHALID UNIVERSITY HOSPITAL, J Hossain, AK Al-Aska, I Al-Orainey, IA Al-Mofleh, RS Al-Rashed, A Ayoola, King Khalid University Hospital

Ten patients (aged, 19-75 y) with liver abscess were studied at King Khalid University Hospital, Riyadh. Nine patients were male and only one was female. Half of the patients were Saudi nationals. Cardinal clinical features were fever, chills, and abdominal tenderness. Seven patients had amebic liver abscess and three had pyogenic liver abscess. Multiple abscesses were noted in two. Medical management with antiamebic agents and antibiotics was successful in five. Five patients required percutaneous catheter drainage. Only 1 patient with multiple pyogenic abscess died. Clinical awareness of liver abscess and early treatment could go a long way to reduce the fatality rate of the disease.

MANAGEMENT OF REFRACTORY ASCITES USING THE RIYADH-ASCITIC-FLUID-ULTRAFILTRATION PUMP, H Abu-Aisha, S Huraib, A Mitwalli, N Ali, A Al-Askar, F Sulimani, M Agraharkar, King Khalid University Hospital, Riyadh

A small percentage of patients with gross ascites can be refractory to the therapeutic effects of potent diuretics even when they are supplemented with albumin infusions. Such patients have been managed by various techniques, including intermittent paracentesis, peritoneovenous shunts, and ascitic fluid ultrafiltration with reinfusion in the peritoneal cavity or blood stream. Each of these methods has its complications and problems. They all become difficult to use when renal insufficiency is associated with the gross ascites. Volume depletion may cause further insult to the renal infusion, whereas peritoneovenous shunts tend to overload the compromised circulatory system. To overcome these problems, we have modified the ascitic fluid ultrafiltration methods in such a way that ascitic fluid is mixed extracorporeally with the patient's blood in an artificial kidney (hollow-fiber membrane) and the mixture is ultrafiltrated and/or dialyzed before it is returned to the venous side of the patient's blood. This method removes free water from the ascitic fluid and returns the colloids to the circulation. The infused back can be controlled fairly accurately. We used this method 12 times in five patients.

CLINICAL PRESENTATION OF NECROTIZING ENTEROCOLITIS (NEC) IN NICU, KING KHALID UNIVERSITY HOSPITAL, RIYADH, (1403-1408H), AMA Abdullah, KN Haque, King Khalid University Hospital, Riyadh

Clinical presentation, diagnostic features, therapeutic measures, and results of treatment of 34 infants with diagnosis of NEC over a 5-year period were reviewed. The overall incidence of NEC in our series is 0.3% (34/11,050). However, in infants who required admission to NICU, it was 3% (34/1100). The mean birth weight was 167 g. Most of the babies were born pre-term. Abdominal distention was present in 77.1% of our patients with NEC, while increased gastric residue and blood in the stool were present in 48.6% and 37.1%, respectively. Twenty percent of the babies had perforation at the time of presentation and/or during their illness. Overall mortality of these cases was 26.4%. Details of this study were presented and results compared with the international literature.

IS SHIGELLOSIS A PROBLEM IN RIYADH?, MW Alam, M Al-Sowailem, A Al-Frayh, M Al-Drou, Riyadh Diarrhoea Centre, Maternity & Children's Hospital, Riyadh

Acute infectious diarrhea is the most serious health problem of children in underdeveloped areas. Although Saudi Arabia is a developing country, the problem is not as acute, though it has immense impact on the child's health and consequently on the physician's attendance. Studies at the Diarrhoea Centre, Riyadh, have shown that among the cases of infectious bacterial diarrhea, *Shigella* (isolated from 8% of the 37,460 routine rectal swabs done on all diarrheal patients reported) was the single most common isolate. Among the serotypes of Shigella, *S. shigae* (the most virulent and invasive strain) was isolated in only three patients. *S.sonnei* and *S. flexneri* (moderately invasive) were the predominant bacterial pathogens (39% and 36%, respectively), followed by *S. boydii* (20%) and *S. dysenterae*, type 2-10 (5%) (both mildly invasive). The most useful signs and symptoms for the diagnosis of shigellosis were fever, abdominal pain/tenesmus with blood and mucus (70% were indicative) in stool, and mild dehydration. Eighty-one percent of *Shigella* cases were resistant to co-trimoxazole; however, ampicillin was still 47% sensitive. Forty-five percent of *Shigella* cases were resistant to both ampicillin and co-trimoxazole, whereas nalidexic acid was 100% sensitive. Ampicillin therefore remains the first drug of choice and nalidexic acid for only those resistant to ampicillin. Random use of nalidexic acid will make it resistant to ampicillin. Random use of nalidexic acid will make it resistant in the future and will leave us perhaps with no alternative to treat this immense problem of shigellosis in Riyadh.

COLON SHIGELLOSIS: SERIAL COLONOSCOPIC APPEARANCES IN SHIGELLA DYSENTERIAE I, T Abdullah, G Javid, R Mahajan, MS Khuroo, Institute of Medical Sciences, Soura Srinagar, India

Twenty-five patients (16 males and nine females; mean age, 24.7 ± 8.4 y) with acute colitis caused by *Shigella dysenteriae* I were studied. Twenty-two patients had weekly colonoscopic examinations until the last procedure revealed normal colonic mucosa. Six abnormal colonoscopic appearances were documented, namely mucosal edema, ulcers, friability, punctate spots, erythematous areas, and luminal exudate. Mucosal edema was the dominant finding in the first week of the disease. Star-shaped mucosal ulcers and friability were observed and were maximal in the second and third week of the disease. Punctate hemorrhagic spots with normal intervening mucosa in patients with minimal constitutional and colonic symptoms was the hallmark of the disease from the fourth week onward. None of the patients showed granularity, cobble-stoning, linear fissures, pseudopolyps, pseudomembrane, or anal lesions. The colonic involvement was subtotal in 20 patients and total in five. The mucosal disease was continuous in the initial stage and became patchy during the later stage of recovery. The mucosal disease lasted for 38.8 ± 12.1 (10-65) days. All the patients followed by serial colonoscopic examinations had eventually normal colonic mucosa.

PREVALENCE AND DIAGNOSIS OF ROTAVIRUS GASTROENTERITIS (GE) AMONG A PRIVATE HOSPITAL PEDIATRIC POPULATION, M El-Shabrawi, G Habib, MI Abu-Jalalah, S Farah, Dr. Bakhsh Hospital, Jeddah

Rotaviruses are now well-established as the leading cause of acute gastroenteritis (GE) in infants and young children throughout the world [Kapikian et al, 1976], but reports of this infection in higher socioeconomic classes in developing countries are scarce. Working at a private hospital in Jeddah, we are privileged to serve a population belonging almost entirely to social classes I, II, and III, among whom this study was conducted. Between June 1987 and November 1988, 54 pediatric patients admitted with watery diarrhea had their stools tested for rotavirus antigen by enzyme immune assay (Rotazyme Kit II, Abbott) or sensitized latex (Slidex Rota Kit, Bio Merieux). Forty patients had positive stool reaction; seven were from social class I, 18 from class II, and 15 from class III. Twenty-two rotavirus patients presented in the "cold" months of the year, and household contacts were affected in three families. Rotavirus GE caused moderate to severe dehydration in 27 patients, fever > 38.3°C (101°F) in 23, leukocytosis (WBC > 10^9/L) in 25, hyponatremia (serum Na < 130 mmol/L), in five, hypokalemia (serum K < 3 mmol/L) in three, and acidosis (plasma bicarbonate < 18 mmol/L) in 34 patients. Such clinical and laboratory findings are not different from those reported with other viral or bacterial enteritides. In conclusion, rotavirus GE is a potentially serious and widely prevalent infection among the higher socioeconomic classes in Jeddah. Family contacts are at risk of infection. Clinical or laboratory features are not pathogenic and fecal assay for rotavirus antigen is the gold standard for diagnosis. Its control seems remote but might be achieved by the development of an effective vaccine.

HYDROGEN BREATH TESTS: FASTING BREATH HYDROGEN LEVELS AND THE EARLY RISE OF BREATH HYDROGEN, AS Dissanayake, HA El-Munshid, A Al-Quorain, HM Al-Freihi, H Al-Idrissi, H Al-Breiki, Y Al-Gindan, College of Medicine, King Saud University, Riyadh

Hydrogen breath tests are routinely used in gastroenterology for the diagnosis of sugar malabsorption, estimation of mouth to cecum transit time (MCTT), and small intestine bacterial growth. Their interpretation is based on a rise in breath hydrogen (BH) above fasting levels after oral ingestion of a sugar substrate. An early rise of BH may confuse the result. A 1% chlorhexidine mouthwash and oral hygiene have been shown to limit this early rise. A fasting breath hydrogen level of > 40 ppm has been considered by some workers to be indicative of gastrointestinal disease. We report here our experience in hydrogen breath testing for the diagnosis of lactose malabsorption and for determining MCTT. The mean fasting BH level in 46 subjects who were lactose absorbers was 7.5 ± 4.8 (no mouthwash) and 8.8 ± 8.2 (N = 31; with mouthwash) compared to levels in lactose malabsorbers in whom it was 10.5 ± 7.2 (N = 40; no mouthwash) and 11.7 ± 9.6 (N d 37; with mouthwash). The mean fasting BH level in 21 patients with irritable bowel syndrome (IBS) was 13.2 ± 9.1. Eleven of the IBS patients had further fasting BH samples taken on two separate occasions four weeks apart, and the mean fasting BH levels were 9.45 ± 8.14 and 10.7 ± 5.9, respectively. The mean fasting level for the lactose malabsorbers and that for the IBS patients were significantly higher than those for the lactose absorbers, supporting the views that patients with GI disturbances tend to have higher fasting BH levels. We also observed that the duration of the fast is an important determinant of the fasting BH level. In three of the IBS patients, high fasting levels were noted; the levels declined when fasting samples were taken a half to one hour later. The mean BH levels 10 minutes after ingestion of lactulose in IBS patients given mouthwash on three separate days was 15.9 ± 10.3 ($P < 0.05$ by Student's paired *t*-test), 13.3 ± 7.3, and 11.8 ± 8.4 compared to the corresponding mean fasting levels of 13.2 ± 9.1, 9.5 ± 8.1, and 10.7 ± 5.9, respectively. In the case of the lactose breath tests, too, the use of the mouthwash tended to limit the early rise in BH. Use of the chlorhexidine mouthwash does not abolish the rise in BH 10 minutes after sugar ingestion but limits it such that interpretation of the test results does not become a problem.

MOUTH TO CECUM TRANSIT TIME IN PATIENTS WITH IRRITABLE BOWEL SYNDROME, HM Al-Freihi, AS Dissanayake, HA El-Munshid, A Al-Quorain, Y Al-Gindan, H Al-Idrissi, E Ibrahim, College of Medicine and Medical Sciences, King Faisal University, Dammam

Irritable bowel syndrome (IBS) is a common gastrointestinal disease of unknown etiology, characterized by abdominal pain and altered bowel habit. Abnormalities of both small intestinal and large intestinal motility have been demonstrated in patients with IBS, by both pressure recording as well as transit time studies. We report our preliminary results in 23 patients (19 males and four females) with IBS. The mouth to cecum transit time (MCTT) was measured using the lactulose breath test. The MCTT may be obtained from a lactulose breath test using three different interpretations of the rise in breath hydrogen. Our data show that there is no significant difference in MCTT between the three methods employed. The mean MCTT in IBS patients ranged from 30 to > 190 minutes with a mean of 86 ± 54 minutes. The overall mean for the group did not differ significantly from the mean of 72 ± 22 minutes for the five controls studied to date. When the IBS patients were divided into two groups: (1) those complaining predominantly of diarrhea and (2) those with constipation or alternating constipation and diarrhea, the mean MCTTs were 43 ± 32 and 101 ± 55 minutes, respectively. These did not differ significantly from the mean for the control group but were significantly different from each other ($P = 0.01$ by Student's t test) and are in agreement with data from other studies. The work is still continuing and we hope to include more controls and patients in the study.

HUMAN DICROCOELIASIS: REPORT OF 208 CASES FROM SAUDI ARABIA, AR El-Shiekh, Armed Forces Hospital, Riyadh

In 3 years, *Dicrocoelium dendriticum* ova were detected in 208 patients at the Armed Forces Hospital, Riyadh. Twenty-three percent of these patients were under 14 years of age. The peak incidence of infestation was between October and November in each of the 3 years. Of these patients, 134 were symptomatic. Sixteen patients had disturbed liver functions and 13 had eosinophilia. Ten patients had gallbladder or biliary tree disease; in at least two of whom it was due to *Dicrocoelium dendriticum*. Malabsorption occurred in one patient. Praziquantel was used in nine patients and was successful in treating four of these patients.

ULCERATIVE COLITIS: THE RIYADH CENTRAL HOSPITAL EXPERIENCE, F Al-Shadoukhy, A Rawshdh, Riyadh Central Hospital

We report our experience with ulcerative colitis (UC) at the Endoscopy Unit at Riyadh Central Hospital. Over the 9-year period (1400-1408H), a total of nearly 1,700 lower gastrointestinal procedures (sigmoidoscopies and colonoscopies) were performed. Histologically proven cases of UC were identified in 87 patients (5.2%). The male to female ratio was 1.12:1 with a mean age of 34 years (range, 7-80). There were 51 Saudi patients (58.6%) with a male to female ratio of 0.82:1 and a mean age of 34 to 33 years; two thirds of the patients were in the 20 to 40 year age range. The distribution of colonic involvement was as follows: proctitis (5.8%), proctosigmoiditis (28.7%), distal colitis (36.8%), and total colitis (28.7%). The clinical and colonoscopic features will be presented. All patients were managed conservatively. Only one patient required surgery for carcinoma of the cecum, diagnosed at the time of colonoscopy in a Saudi patient with total colitis. No extraintestinal complications were noted, apart from one case associated with chronic active hepatitis and another with primary sclerosing cholangitis. We conclude that UC is not uncommon in Saudi Arabia. The disease seems to take a more benign course than that described from the West.

CHRON'S DISEASE IN ARABS, J Hossain, RS Al-Rashed, FZ Al-Faleh, IA Al-Mofleh, King Khalid University Hospital, Riyadh

Nine patients with Chron's disease were observed in two teaching hospitals in Riyadh between 1403 and 1409H. Among them, eight patients were Arabs. Four were Saudi nationals (three female, one male). Age ranged from 18 to 35 years. Cardinal clinical features were abdominal pain, chronic diarrhea, weight loss, and fever. Physical examination showed abdominal tenderness in seven patients and mass lesions in the abdomen in two patients. Ileocolic disease was noted in only four, ileal involvement in one patient, and colonic involvement in three patients. Surgery was performed in five patients for therapeutic and diagnostic purposes. Extraintestinal manifestations were noted in three patients. Relapse of the disease was noted in one patient. Two patients required parenteral nutrition and seven patients were treated with short-term corticosteroid treatment. Follow-up was between 1 to 5 years. Three patients were lost to follow-up. No patient had malignant changes. Chron's disease may be rare in Arabs, but it does exist.

COLO-RECTAL MALIGNANCIES IN RIYADH CENTRAL HOSPITAL, MI Sebayel, AD Dohayan, QO Al-Qasabi, RC Tandon, MA Al-Mofarreh, A Al-Kraida, Riyadh Central Hospital and King Khalid University Hospital Hospital, Riyadh

Colorectal carcinoma is the second most common visceral cancer in the West, accounting for approximately 13% of all cancer deaths. While the incidence seems to be much less in developing countries, it is not unknown. We undertook this study of all colorectal cancer patients admitted to Riyadh Central Hospital during 1405-1408H, with the aim of analyzing their presenting features as well as some of the epidemiologic factors. The total number of patients was 110; 57 were colonic and 53 were rectal. The male to female ratio in colonic cancer was 2.3:1 (1:1.2 in the West), while in rectal cancer this was 1.5:1. Another interesting feature which emerged was the higher number of patients under the age of 40 (31.3%) in comparison to the West (8%). Saudi nationals constituted 54% of the total number. Of these 110 patients, two had lymphoma of the colon and one had carcinoid tumor. Predisposing conditions included polyposis coli in one patient and ulcerative colitis in another. Right-sided colon was involved in 35.5%, left-sided (rectum and sigmoid) in 60%, and transverse in 4.5%. Benign anorectal diseases constitute almost 30% of our outpatient attendance, but cancer is very low. Animal fat ingestion is very high in Saudi Arabia, and with the economic change, consumption of processed food has also increased. These two factors may lead to an increase in the incidence of colorectal disease in this country in the coming 10 to 20 years. Our follow-up is not adequate, partially because of failure of attendance on the part of the patients and partially because non-Saudis constituted a good percentage.

CONGENITAL MEGACOLON: SURGICAL VERSUS MEDICAL MANAGEMENT, SA Saad, King Faisal Specialist Hospital and Research Centre, Riyadh

Congenital megacolon or Hirschsprung's disease is a congenital anomaly characterized by partial or complete large bowel and possible small bowel obstruction due to the lack of intramural ganglion cells from the involved GI tract. The diagnosis of congenital megacolon should be suspected in the first few days of life. However, many cases are diagnosed later. The treatment of congenital megacolon, after confirming diagnosis with rectal biopsy, is surgical. Management of congenital megacolon by medical means using Fleets enema and rectal dilations is very harmful and is associated with high morbidity, such as fulminating enterocolitis and high mortality in up to 90% of cases. On the other hand, management of Hirschsprung's disease with surgical means by initial colostomy and subsequent pullthrough procedure is curative and is associated with satisfactory morbidity and very low mortality. This paper described the steps in diagnosing congenital megacolon and compared the results of medical and surgical management.

HEPATIC SCHISTOSOMIASIS, MA Madwar, Ain Shams University, Abbassia, Cairo, Egypt

Hepatic schistosomiasis is a chronic disease of the liver characterized by granulomatous reaction, portal fibrosis, and presinusoidal portal hypertension. *Schistosoma* eggs and subsequent fibrosis are the causative factors of hepatic pathology. The disease is progressive if not treated early. Liver functions remain within normal limits until a very late stage. Early in the disease, there is hyperplasia of reticuloendothelial cells of the spleen, leading to its enlargement. Later there is congestive splenomegaly. HLA haptotypes A_1 and B_5 were present in high frequency in a group of children who had hepatomegaly.

MANAGEMENT OF PORTAL HYPERTENSION, AA Salam, Emory University, Atlanta, Georgia, U.S.A.

When to sclerose? When to operate? A shunting or nonshunting procedure? If shunting, what shunt? When to transplant? The author discussed these hotly contested and debated issues by reviewing his experience and that of others over the last three decades. The lessons learned in the sixties, seventies, and eighties were critically analyzed, and on the basis of this analysis, specific recommendations for treatment of portal hypertension were made.

LOCAL EXPERIENCE IN THE SURGICAL MANAGEMENT OF PORTAL HYPERTENSION, A Al-Kraida, S Qazi, M Al-Mofarreh, R Al-Ariyan, Riyadh Central Hospital

Upper gastrointestinal tract bleeding in patients at Riyadh Central Hospital is a common surgical problem, so much so that, we have a special unit (Haematemesis and Melaena Unit) where all such patients are admitted for resuscitation, assessment, and further management. Nearly one third of cases consist of bleeding esophageal varices due to portal hypertension. Most are due to schistosomiasis or posthepatic type. All patients with a recent history of significant bleeding esophageal varices are offered surgery. We adopted transabdominal devascularization, splenectomy, and esophageal transection with EEA staplers as the surgical treatment. One hundred twenty patients underwent this procedure over the last three and a half years. During a follow-up period of 2 to 3 years, the patients did not show any rebleeding. No leak from the esophageal transection site was observed, but 4% developed gastric leaks and were managed successfully with conservative treatment. Five percent of the patients developed temporary dysphagia while 2% developed esophageal stricture which responded to endoscopic dilations. Postoperative mortality rate of 10% due to hepatic and hepatorenal failure is recorded. The satisfactory outcome of combined gastroesophageal devascularization and esophageal transection for bleeding esophageal varices has encouraged us to persist with the method.

HEPATOCELLULAR CARCINOMA (HCC): INTERNATIONAL ASPECTS, YM Fakunle, Riyadh Central Hospital

HCC is one of the world's most common malignancies. The annual incidence is on the order of 250,000 cases. Unless detected early and surgically resected, death ensues usually within 6 months of diagnosis. There are striking differences in the age of onset, prevalence, and proportion of tumors secreting alpha-fetoprotein (AFP) in different parts of the world. In high-incidence areas, exemplified by Southeast Asia and the black community of Southern Africa and West Africa, the prevalence rate may be as high as 50 to 150/100,000 population, and the tumor presents at a young age (less than 35 years). In low-incidence areas, such as the U.K., Canada, and Australia, prevalence is less than 4/100,000 and the mean age at presentation is 50 years or older. There is a remarkable male preponderance and association with chronic hepatitis B virus infection and cirrhosis worldwide. Population studies in widely separated geographical areas in Africa also suggest a correlation between aflatoxin exposure and HCC. In Saudi Arabia, the prevalence of HCC is several times higher than in the Western hemisphere and constitutes between 12 and 20% of all digestive neoplasms, compared with 2% in the U.S. Also, in contrast to Western Europe, primary carcinoma outnumbers metastatic carcinoma 7 to 1 in Saudi Arabia. However, the age of onset of HCC in Saudi Arabian patients seems to be similar to that in races of low incidence. Patients were rarely younger than 35 years old in contrast to African and South East Asian patients. To obtain data for detailed international comparison of the epidemiology and other aspects of HCC, a cancer registry should be established in the Kingdom.

PRIMARY HEPATOCELLULAR CARCINOMA IN THE WESTERN REGION OF SAUDI ARABIA, O Shobokshi, King Abdulaziz University, Jeddah

A remarkable geographic variation of primary hepatocellular carcinoma (PHC) is known to exist worldwide. However, in the Middle East little information on PHC is available due to lack of proper epidemiologic study, valid medical statistics, and a cancer registry. A high incidence of 10 to 20% HBsAg carrier rates has been reported from various regions of Saudi Arabia. With the unusually high incidence of hepatitis B virus carriage reported among PHC patients worldwide, this project was designed to prospectively determine: (a) the size of the problem of PHC in our community; (b) the etiologic factors; and (c) recommendations for primarily preventing the disease. For the above objectives to be achieved, 200 histologically proven PHC patients, recruited from various hospitals in Jeddah and Gizan, were examined clinically, and sera and liver biopsies were analyzed immunologically and histopathologically, respectively, over a 3-year period. Matched control groups comprising 200 healthy HBsAg carriers, 106 patients with other neoplasms, and 3,323 normal Saudis were compared to the PHC group. Among the tests used were various routine and immunoperoxidase histologic stains, ELISA, immunofluorescence and radioimmunoassays, or liver biopsies and sera, as well as other procedures such as x-ray studies.

MRI OF THE LIVER, DC Clark, Armed Forces Hospital, Riyadh

The advantages of MR over CT, including superior soft tissue differentiation and multiplanar imaging, have made MR the imaging method of choice in the CNS. However, progress in

MR imaging of the abdomen has been hindered by the image degradation produced by physiologic motion. Numerous ways to reduce this problem have been tried, but to date none is completely satisfactory. Despite this, MR still is useful for abdominal imaging, particularly of the liver. The most commonly used MR technique is the splenoecho technique in which most (but not all) liver pathology will appear dark on T_1-weighted images and bright on T_2-weighted images. Present evidence suggests that at low to medium field strength (0.15T to 0.6T), T_1-weighted images produce better lesion for liver contrast, while at higher field strength (over 1.0T), T_2-weighted images may be better. Most malignant tumors of the liver, both primary and secondary, appear as dark regions on T_1-weighted images and bright areas on T_2-weighted images. The most common benign liver tumor, the cavernous hemangioma, has a characteristic hyperintense appearance on T_2-weighted images which allows it to be differentiated from malignant lesions in over 90% of the cases. Vascular anatomy is often well shown by MR, since in the spin-echo technique, rapidly flowing blood will produce no signal, thus the splenoportal venous system can be assessed and the presence of varices detected. MR has also been used in the pre- and postoperative assessment of vessels. Iron deposition in the liver is particularly suitable for MRI, since the presence of iron causes a marked diminution of signal from the affected liver. This phenomenon may prove useful in the use of iron particles as a contrast agent.

LIVER TRANSPLANTATION, DH Van Thiel, School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, U.S.A.

As of this writing, nearly 3,000 liver transplants have been performed in the U.S. alone, and probably another 1,000 elsewhere in the world. There are two different methods of liver transplantation. The first consists of insertion of an extra liver (auxiliary liver transplantation) at an ectopic location. The second is orthotopic liver transplantation. Results of auxiliary transplantation have been disappointing. Although the orthotopic approach produced initially disappointing results, with continued experience, it became clear that it was a technically easier method for some hepatic diseases. These can be grouped into four major categories: chronic advanced irreversible liver disease, hepatic malignant neoplasm, fulminant hepatic failure, and inborn errors of metabolism. Results have been better in children (5-year survival, 85 to 90%) than in adults (5-year survival, 55 to 85%). However, all patients being considered for liver transplantation should be carefully evaluated for indications (e.g., advanced excretory, synthetic, or metabolic abnormalities of liver disease; advanced symptomatic liver disease) and contraindications (e.g., active sepsis outside the hepatobiliary tree, metastatic hepatobiliary malignant neoplasm, advanced cardiopulmonary disease, AIDS).

EXTRACORPOREAL SHOCKWAVE THERAPY OF GALLBLADDER STONES, M Sackmann, University of Munich, West Germany

Extracorporeal shockwave lithotripsy combined with adjuvant bile acid therapy (ursodeoxycholic acid and chenodeoxycholic acid) have been introduced for the treatment of symptomatic gallbladder stones [N Engl J Med, 1986]. Initial clinical experience in the first 175 patients revealed safety and efficacy of this novel, nonoperative technique [N Engl J Med, 1988]. To further substantiate our initial experience, we have now treated more than 500 patients by extracorporeal lithotripsy. With an advanced-technology lithotriptor (MPL 9000, Dornier), general or epidural anesthesia is not required; they have been replaced by intravenous, or even no, analgesia. All patients received adjuvant litholytic bile acid therapy with ursodeoxycholic acid and chenodeoxycholic acid (7.5 mg/kg/d) started 2 weeks prior to lithotripsy and continued for 3 months beyond complete clearance of all fragments. Of the patients with one to three radiolucent stones less than 3 cm in diameter in a functioning gallbladder, more than 80% can be expected to be completely stone free 1 year after lithotripsy, according to actuarial analysis. Severe complications were rare: 1% mild pancreatitis; elective cholecystectomy in 1%. It is concluded that extracorporeal shockwave lithotripsy combined with adjuvant bile acid therapy is a safe and effective nonoperative therapy for selected patients with radiolucent gallbladder calculi.

EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY AS AN ADJUNCT IN THE TREATMENT OF BILE DUCT STONES, M Sackmann, University of Munich, West Germany

Endoscopic sphincterotomy and stone extraction result in complete clearance of the bile ducts from stone obstruction in about 80 to 90% of the patients. For the few patients in whom endoscopy fails, open abdominal surgery has been the only alternative in these mostly old and severely ill patients. Therefore, we have attempted to evaluate the role of extracorporeal lithotripsy for disintegration of bile duct stones which could not be extracted endoscopically after sphincterotomy. We have treated more than 70 patients with bile duct stones not amenable to endoscopic measures. Using a common kidney stone lithotriptor (HM3 or HM4, Dornier) with a radiologic stone positioning system, or in the case of intrahepatic calculi, the gallstone lithotriptor MPL 9000 with ultrasonographic stone identification system, sufficient fragmentation was achieved in 80% of the patients. Thereafter, the fragments were either passed spontaneously or were extractable by endoscopic measures after disintegration. One case of acute cholecystitis was the only acute complication. It is concluded that extracorporeal lithotripsy is a helpful adjunct to the nonoperative techniques applied for bile duct stones.

ACUTE PANCREATITIS: HIGHLIGHTS OF DIAGNOSIS, H Al-Freihi, King Faisal University, Dammam

Acute pancreatitis is believed to be an autodigestive disease of unknown etiology. Activated pancreatic digestive enzymes have been found within the pancreas. Pancreatitis has been associated with a number of conditions considered the cause of acute pancreatitis. Signs and symptoms associated with acute pancreatitis could not easily be differentiated in general from a number of conditions like perforated viscus, ruptured aortic aneurysm, mesenteric infarction, rupture of ectopic pregnancy, etc. This picture is further complicated by the fact that all of these conditions and others give rise to hyperamylasemia. The presence of certain physical signs such as subcutaneous flank or paraumbilical hemorrhages (Grey Turner's, Cullen's sign) and erythematous nodules on the extremities suggest pancreatitis. Further, differentiation of pancreatitis, particularly the chronic type, from neoplasm of the pancreas can sometimes be difficult even after application of invasive diagnostic techniques. There are various secretagogues which stimulate the pancreatic acinar cells to release enzymes by binding to certain receptors, activating one of two functionally distinct processes. One of these utilizes intracellular calcium while the other activates adenylate cyclase. Enzymes and zymogens are stored in granules and discharged into the pancreatic ducts upon stimulation. Pancreatic juice consists of two components: $NaHCO_3$ and about twenty different digestive enzymes and co-factors. Release of these components is controlled by nearly forty regulatory peptides. These facts have been utilized in part to diagnose some of the pancreatic diseases. Among the laboratory diagnostic tests, determination of serum amylase is the most widely used. However, this test has many drawbacks, as amylase is produced in a number of organs, elevated in certain abdominal and extraabdominal diseases, and has a short serum half life. In general, it is accepted that a transient elevation of amylase to at least three times the upper limit of normal is indicative of acute pancreatitis. Electrophoretic separation of the amylase into pancreatic and salivary components has improved its diagnostic value. A pancreatic isoamylase fraction of > 0.75 of the total is suggestive of acute pancreatitis and could rule out 44% of cases with acute abdomen and elevated amylase [BW Pace et al, 1985]. Determination of other enzymes like lipase, immunoreactive trypsin, and elastase 1 seems to be more specific than total amylase but equal to P-isoamylase. Elastase 1 and trypsin remain elevated longer than the other enzymes, and therefore are useful in the diagnosis of cases when there is a delay between the onset of symptoms and admission [B Flamion et al, 1987]. Furthermore, there are assays which are not yet widely used, and therefore their sensitivity and specificity could not be established. These tests include carboxypeptidases A and B and phospholipase A_2. The serum levels of the assays mentioned so far do not correlate with the severity, and thus the prognosis of acute pancreatitis. Tests claimed to predict severity, but not yet confirmed, include serum ribonuclease, alpha-2-macroglobulin, and alpha-1-antitrypsin-trypsin complex [Warshaw AL, 1979, and Lasson A, 1984]. Therefore, it is better to resort to currently available markers, such as Ranson's prognostic signs [Ranson JMC, 1974 and 1982] or simplified prognostic criteria [Pitchmoni et al, 1988] to assess severity. Determination of the serum level of a carbohydate antigen (monosialoganglioside) CA 19-9 is useful in differentiating pancreatic inflammatory disease from carcinoma of the pancreas, which sometimes proves to be difficult without laparotomy [Piantino P et al, 1986]. Utilization of radiologic examinations, such as plain films of the chest and abdomen, ultrasonography, computed tomography, and more recently, magnetic resonance imaging, has enhanced our capabilities to accurately diagnose acute pancreatitis and more so its complications. Performance of endoscopic retrograde cholangiopancreatography (ERCP) within the first 24 to 48 hours is controversial, as ERCP by itself can cause acute pancreatitis. However, in certain conditions such as trauma or gallstone-related and recurrent acute pancreatitis, ERCP has important diagnostic, therapeutic, and prognostic value.

TREATMENT OF ACUTE PANCREATITIS AND ITS LATE COMPLICATIONS, AA Salam, Emory University Hospital, Atlanta, Georgia, U.S.A.

Despite vast improvement in the management of critically ill patients, acute pancreatitis remains a highly lethal disease. Patients who survive the acute episode remain at risk of developing late complications which often require surgical intervention. These complications include pseudocysts, pancreatic biliary obstruction, duodenal obstruction, and hemorrhage. The author discussed the diagnosis and management of acute pancreatitis with particular emphasis on the role of peritoneal dialysis and the management of pancreatic sepsis. He also discussed the late complications of pancreatitis using case histories to illustrate the role of newer diagnostic techniques in the management of these difficult problems.

ABNORMAL TERMINATION OF THE COMMON BILE DUCT: THE SAUDI EXPERIENCE, SA El-Boghdadly, DL Glen, MF Seraj El-Deine, King Fahad National Guard Hospital, Riyadh

The termination of the common bile duct (CBD) in the duodenum is of great interest to endoscopists, radiologists, and surgeons. The ever-increasing endoscopic and surgical procedures around the duodenal papilla necessitate a better understanding of the anatomy of the common bile duct. However, there has been scant attention in the literature about the termination of the CBD. The operative cholangiograms of 126 patients were reviewed separately by two surgeons and a radiologist to determine the site of termination of the CBD. The CBD was noted to terminate in its normal position at the second part of the duodenum in 92 patients (72.02%); there was abnormal termination in the junction of the second and third part of the duodenum in 16 patients (12.7%); eight patients' CBD terminated in the junction of the first and second part of the duodenum; and seven patients' (5.6%) CBD terminated in the third part of the duodenum. The pancreatic duct was outlined in 37 patients (29.37%).

CAROLI'S DISEASE: RIYADH CENTRAL HOSPITAL EXPERIENCE, SA Qazi, AA Al-Kraida, MA Al-Mofarreh, G Atilio, Riyadh Central Hospital

Caroli's disease is characterized by congenital saccular dilatations of intrahepatic bile ducts involving a segment, sector and lobe, or both lobes of the liver. Biliary stasis leads to biliary lithiasis, and, if untreated, to suppurative cholangitis, septicemia, intra- and extrahepatic abscesses, and carcinoma. Since 1985, we have seen seven cases of Caroli's disease in our hospital. Age ranged from 11 to 50 years. The disease has been mostly confined to one lobe of the liver. Association of congenital hepatic fibrosis with portal hypertension is recorded in one case and medullary sponge kidney in one. Four patients had left hepatic lobectomy, and in one patient, bleeding esophageal varices necessitated esophageal stapling transection as the first line of treatment. The disease must be recognized before life-threatening complications arise. The new hepatobiliary imaging procedures now allow early diagnosis and better therapeutic approaches in many cases. Hepatic resectional surgery in patients with localized lobar involvement should be the treatment of choice.

ROLE OF ERCP IN THE MANAGEMENT OF SYMPTOMATIC POST-CHOLECYSTECTOMY PATIENT, M Al-Mofarreh, MA Al-Moagel, AQM Mohsen, A Al-Kraida, NM Tikku, AA Mohamed, Riyadh Central Hospital

Retained stones and/or recurrence of symptoms is a well-known sequela after biliary surgery. During the period 1405 to 1408H (1985-1988), 136 patients were referred to the Endoscopy Unit of Riyadh Central Hospital because of symptoms related to the biliary tract. The duration of symptoms ranged from a few days to years after cholecystectomy. 43.4% of patients had stones in the biliary tree; 41.2% had other pancreatobiliary pathology; and 15.4% showed a normal biliary tree. Various therapeutic procedures were undertaken in most of the cases, and only a few were subjected to surgery. We found that endoscopic retrograde cholangiopancreatography is a very suitable procedure for evaluating symptomatic post-cholecystectomy patients, and therapeutic intervention solves most of their related problems.

SPHINCTER OF ODDI DYSFUNCTION: CLINICAL AND MANOMETRIC STUDY WITH EVALUATION OF DRUG THERAPY WITH NIFEDIPINE, MS Khuroo, SA Zargar, R Mahajan, Riyadh Armed Forces Hospital

With the advent of endoscopic retrograde cholangiopancreatography (ERCP), and some added refinements, it has become possible to do manometric assessments of the sphincter of Oddi (SO) in normal and abnormal states. Evidence has accumulated that patients with biliary and/or pancreatic symptoms of unexplained cause have abnormal SO pressures or responses to pharmacologic agents. To investigate this further, SO manometry was carried out to test the response to morphine, nifedipine, scopolamine, and butylbromide. Morphine sulfate (3 mg IV) increased the frequency of phasic activity but had no significant effect on the amplitude of ductal pressure (SO basal or phasic contraction). Nifedipine (10 mg sublingually) had a predictably slow effect on SO, starting within 5 minutes and extending up to 15 minutes. It reduced the frequency of SO activity, as well as the amplitude of basal and phase contractions. Nifedipine is therefore a more useful drug in the treatment of biliary dykinesia. Butylbromide (40 mg IV) had a dramatic effect on SO activity, starting within 30 seconds and lasting 5 to 10 minutes. It abolished phasic activity of SO and the bile duct duodenal pressure gradient. Therefore, butylbromide is a good agent for relief of symptomatic episodes of SO dysfunction, but is not suitable for long-term treatment. The characteristics of SO with endoscopic sphincterotomy can be divided into three subgroups: Group 1: papilla with minimal fibrosis or deformity; SO diameter at 2 years, 60% of the original diameter; SO manometry reveals no sphincteric basal or phasic activity and no duodenal bile duct pressure gradient. Group 2: papilla with considerable deformity but minimal fibrosis; SO diameter at 2 years, 30% of the original diameter; SO manometry reveals resurgence of basal and phasic activity of SO and development of duodenal bile duct pressure gradient. Group 3: papilla with considerable fibrosis and deformity; SO diameter at 2 years, 20% of the original diameter; SO manometry reveals a high basal SO pressure without phasic activity and high duodenal bile duct pressure gradient, the so-called sphincteric stenosis. Two disease states are potential candidates for definition of SO dysfunction: post-cholecystectomy biliary dyskinesia, and recurrent acute pancreatitis of undefined cause.

EXPERIENCE WITH BILIARY STRICTURES FOLLOWING A RECENT CHOLECYSTECTOMY, SI Suleiman, Security Forces Hospital, Riyadh

A group of 28 consecutive patients who developed biliary strictures following cholecystectomy were studied. Of the 28 patients, ten had common bile duct exploration and one had a hepaticojejunostomy during the cholecystectomy operation. Of the 28 patients, 22 gave a history of blood transfusion The referral notes were complete in 22 patients, 20 of whom received 2 to 12 units of blood (mean, 4 units). Only four had a record of a peroperative cholangiogram. All patients were referred with jaundice 3 to 8 weeks following cholecystectomy. Only two patients gave a history of jaundice prior to surgery. All patients had their biliary trees opacified by percutaneous transhepatic cholangiography and/or endoscopic retrograde cholangiopancreatography, confirming the presence of the strictures. Of the 28 patients, 27 underwent laparotomy; hepaticojejunostomy was performed in 19; mucosal grafting for high strictures in six; mucosal graft to the right hepatic duct in one; and common bile duct reconstruction in one. The remaining patients had the hepaticojejunostomy stoma visualized by a small intestinal fibroscope. Biliary fluid was flushed away by saline and gentamycin. From this group of patients, it can be seen that it is the difficult cholecystectomy that is followed by early postoperative stricture, and that perhaps bleeding is the cause of injury. Choledochoscopy and peroperative cholangiogram should be routine throughout the Kingdom.

RETAINED BILIARY CALCULI WITH T TUBE IN SITU: ENDOSCOPIC MANAGEMENT, M Al-Mofarreh, MA Al-Moagel, AQM Mohsen, AA Mohamed, NM Tikku, Riyadh Central Hospital

Retained common bile duct (CBD) stone is one of the common drawbacks in biliary surgery for calcular disease. Early diagnosis is possible if the T tube remains in situ after the surgery and a cholangiogram done peroperatively. Various therapeutic modalities have been adopted to clear up the stone. Thirty-five patients were referred to the Gastroenterology Unit of Riyadh Central Hospital with retained CBD stones, along with in situ T tube, during 1405 to 1408H (1985-1988). Stones were extracted from the biliary tree with Dormia basket. Some small stones were passed spontaneously after papillotomy. Mechanical lithotripsy was successfully performed in one patient. We found that technically it is feasible to extract stones without much difficulty from the biliary tree despite the in situ T tube. One of the advantages is that the biliary tree can be seen later, so that retained stones can be searched for, even after extraction, without the need for invasive procedures. We did not encounter any complications.

BILIARY AND PANCREATIC ASCARIASIS: LONG-TERM FOLLOW-UP OF 11 PATIENTS, T Abdullah, G Javid, R Mahajan, MS Khuroo, Institute of Medical Sciences, Soura Srinagar, India

From December 1982 to January 1988, 420 cases of biliary and/or pancreatic disease related to ascariasis were diagnosed. One hundred ten patients had adult worm seen in the biliary tract or pancreatic duct at endoscopic retrograde cholangiopancreatography (ERCP), 250 patients had suspected recent biliary invasion as per established criteria [Gastroenterology 1985;88:418-23], and 60 patients had primary bile and hepatic duct calculi with worm fragments forming their nidus, as seen in histologic examination of the stone. The present paper deals with a 5-year follow-up of 110 patients with biliary and/or pancreatic ascariasis. Of the 110 patients, one patient with pancreatic ascariasis died with severe pancreatitis and 11 other patients were operated on because of coexistent bile duct calculi. Ninety-eight patients showed apparent clinical recovery: of these, 52 were reassessed at 3 weeks. Worms had not moved out of the bile duct in 47 patients or out of the pancreatic duct in five patients. Of the 98 patients followed-up, 24 had recurrence of symptoms. Thirty-seven symptomatic episodes (biliary colic, 15; pyogenic cholangitis, 20; acute pancreatitis, two) were recorded over a mean follow-up of 36.0 ± 13 mo (range, 1 to 59 mo). Twenty-two such relapses were assessed by ERCP; 16 were related to biliary worm re-invasion, five to formation of biliary calculi, and one to biliary worm re-invasion; nine had had previous surgical/endoscopic manipulations of the papilla, causing widened passage. One patient with biliary worm re-invasion died with severe pancreatitis. Histologic examination of biliary calculi in 16 patients revealed worm or worm fragments of the nidus with mineral deposits over them. The paper stresses the magnitude of biliary and pancreatic disease due to ascariasis in endemic areas. The natural history of biliary ascariasis is fraught with frequent recurrences due to worm reinfection and biliary re-invasion, and high occurrence of primary and hepatic duct calculi.

ACUTE PANCREATITIS IN RIYADH, MA Laajam, College of Medicine, King Saud University, Riyadh

This was a retrospective study of all cases of acute pancreatitis (AP) admitted consecutively to the University Hospitals in Riyadh over the 5-year period, 1404-1408H (1984-1988). The aim of the study was to identify the causes and characterize the clinical spectrum of AP in Saudi Arabia. A total of 104 attacks of AP in 91 patients were analyzed. The female to male ratio was 1.5:1, with a mean age of 42.4 years (range, 16-74). In 70% of the cases, AP was associated with biliary disease. The etiology was unknown in only 14% of the patients. There were 50 (55%) Saudi nationals among the group, two-thirds of whom were females. In 76% of this subgroup, the AP was associated with biliary disease. Only 2/32 of the Saudi female patients had nonbiliary etiology. Ultrasonography was accurate in diagnosing biliary stones in 60/64 of the biliary-associated AP cases. Thirty-seven percent of biliary pancreatitis patients underwent emergency cholecystectomy and 35% elective cholecystectomy, and no record of surgery at our hospitals could be obtained for the rest. There were three fatal cases in our series, giving a mortality of 3.3%. The underlying etiologies in these cases were: one alcohol abuse, one postoperative (cholecystectomy), and one idiopathic. In conclusion, AP in Saudi Arabia is predominantly biliary-associated, affecting females mostly (particularly among Saudi patients). The disease follows a more benign course and has a lower mortality than that seen in the West.

A PROSPECTIVE STUDY IN THE MANAGEMENT OF ACUTE PANCREATITIS, QO Al-Qasabi, College of Medicine, King Saud University

This prospective study in the management of 114 (66F, 48M) cases of acute pancreatitis utilized Ranson's criteria in the assessment of the severity of the disease, and compared its correlation to the prognosis. Sixty-two of the patients were Saudi nationals. Hyperamylasemia remains at the top of the diagnostic index of acute pancreatitis, and ultrasound accurately detected the stones. Diminution of hematocrit, elevated LDH, age more than 55 years, raised SGOT, and elevated white cell count were the most consistent of Ranson's criteria, in descending order. There were 63 patients who had mild pancreatitis (less than 3 of Ranson's factors), 44 with severe pancreatitis (3-4 factors), six with very severe pancreatitis (5-6 factors), and fatal pancreatitis in one case (more than 6 factors). The incidence of biliary pancreatitis (62 patients; 54.38%) is much higher compared to the low incidence of alcohol-induced pancreatitis (7%) found in the West. Low-grade fever (29%) and jaundice (23.5%) are commonly associated. Epigastric pain (91%) and vomiting (73.5%) are the most common presenting features. Although it is accepted that surgical correction of the biliary tract disease is indicated in biliary pancreatitis, the timing of the procedure is controversial. In this study, 49 of 62 patients with biliary pancreatitis had operative management. The number of complications was low and mortality was 5.26%. Early surgery and endoscopic retrograde cholangiopancreatography probably both played a role in the low morbidity and mortality.

SURGERY IN GALLSTONE PANCREATITIS, SS Ahmed, King Fahd Armed Forces Hospital, Jeddah

Gallstone pancreatitis was the most common type of pancreatitis and was diagnosed in 43 patients during the last 5 years. The pancreatitis was diagnosed by high serum amylase levels in clinically suspected cases, radiologically with CT scanning or during acute biliary surgery. The presence of gallstones was confirmed preoperatively either by radiology or mostly by ultrasonography. One patient from another hospital whose condition deteriorated on admission, with hemodynamic instability, needed intubation and operation. Two patients opted to go back to their home cities for surgery and another had delayed surgery. Another 40 had no hemodynamic instability preoperatively, and only one more had temporary postoperative instability. Five had severe pancreatitis according to the Glasgow scale. Forty patients were operated on with routine operative cholangiogram within 72 hours to 10 days of admission. Thirty-six patients had an inflamed gallbladder containing stones. Four had associated stones in the common bile duct. There was edema of the covering peritoneum with occasional fat necrosis in most cases; there was gross edema of the whole pancreas in seven cases shown by CT preoperatively. There was a minimal amount of clear fluid in three cases, but even in the intubated patient with preoperative hemodynamic instability, there was no pancreatic necrosis or hemorrhagic fluid. Bile culture was positive in only two, perhaps because of peroperative prophylactic antibiotics. All had satisfactory recovery except one unstable patient who was transferred to another hospital while recovering, at the family's request. Four patients were admitted with a history of recurrent attacks of pancreatitis; three had pseudocysts, two required internal drainage, one reabsorbed, and the fourth patient was jaundiced due to stricture of the common bile duct (CBD) resulting from recurrent attacks, and had to be bypassed. We are commonly finding pancreatitis in the mild form, with no actual pancreatic necrosis and rarely hemodynamic instability. We are also finding pancreatitis associated mainly with stones in acutely inflamed gallbladder (only 10% had CBD stone); also, early surgical intervention with routine operative cholangiogram within days of admission when the patient's condition is stable and enzymes are returning to near normal is proving economical and gratifying.

ALPHA-1-ANTITRYPSIN IN PATHOLOGY OF THE GASTROINTESTINAL TRACT, MAF El-Hazmi, AS Warsy, College of Medicine, King Saud University, Riyadh

Alpha-1-antitrypsin (alpha-1-AT), the major protease inhibitor in human plasma, is a glycoprotein with the ability to inactivate a wide variety of endogenous proteases and hence provide protection against their hydrolytic effect. It occurs as different phenotypes that may or may not affect its inhibitory capacity. Several deficient variants have been implicated as a predisposing factor to emphysema and neonatal hepatitis. Association between alpha-1-AT deficiency and hepatocellular carcinoma in adults has been shown in some populations, though in others no specific association has been demonstrated. The increased susceptibility of hepatocytes is believed to result from accumulation of alpha-1-AT-deficient variants as specific globules in the hepatocytes, and this renders the liver cells more susceptible to damage by additional factors. In addition, elevated levels of alpha-1-AT have been demonstrated in several clinical conditions, implicating alpha-1-AT as an "acute phase reactant protein." Pilot studies have shown the presence of alpha-1-AT deficiency in the Saudi population, and we have identified several cases that had less than 20% of the normal "trypsin inhibitory capacity." This paper reports the investigations of alpha-1-AT concentration in plasma, its trypsin inhibitory capacity, and phenotypes in patients with and without liver diseases and other gastrointestinal disorders.

COLONIC AND GASTRIC TRANSPOSITION FOR ESOPHAGEAL REPLACEMENT IN CHILDHOOD, AYI Al-Samarrai, King Khalid University Hospital, Riyadh

The vast majority of infants with esophageal atresia can be successfully treated by primary esophagoesophageal anastomosis. However, 10 to 20% of patients with esophageal atresia are known to have a large gap, making the anastomosis between the proximal and distal ends of the esophagus very difficult. The most popular procedure to bridge the wide gap is delayed primary anastomosis, with or without esophageal elongation, by bougienage and Livaditis circular esophageal myotomy. However, this is still not possible in a certain number of babies for whom division of the tracheoesophageal fistula (TOF) with cervical esophagostomy and feeding gastrostomy is performed as a life-saving procedure—for example, in cases of extreme prematurity or where there is an associated life-threatening congenital anomaly, or where prolonged suction of the upper pouch cannot be safely continued because of inadequate nursing facilities. For these babies, staged surgery is preferable and different organs have been used to reconstruct the esophagus, the commonest being the colon and stomach. In this paper, three infants who presented with long-gap esophageal atresia and TOF were initially treated in King Khalid University Hospital by division of the fistula, gastrostomy, and cervical esophagostomy. A year later, the colon (in one patient) and the whole stomach (in two patients) was used to replace the esophagus. One patient had herniation of the small bowel into the chest six months after surgery, through the old esophageal hiatus. This required surgical intervention. All patients showed normal growth and developmental patterns over the 2 to 4 years following surgery.

ROLE OF DILATION IN THE MANAGEMENT OF BENIGN AND MALIGNANT ESOPHAGEAL STRICTURES, AE Mohamed, MA Al-Karawi, Riyadh Armed Forces Hospital

At the gastroenterology department, Riyadh Armed Forces Hospital, 15,782 endoscopic procedures were performed between January 1982 and October 1988. Of these, 193 esophageal dilations were performed on 74 patients. Thirty-three of these patients had malignant strictures and 41 had benign strictures, the commonest of which was due to esophagitis. Different types of dilators were used, of which Savary dilators were used 104 times. The number of dilations per patient ranged from one to 12. Dilations under fluoroscopy screening were done in some patients. In about 60% of the patients, dysphagia improved following first-third set of dilation. In 16 patients with malignant strictures, tube insertion was performed, including feeding tubes or Atkinson tubes. Failure of dilation occurred in two patients and failure of tube insertion in another two. Esophageal perforation as a complication following dilation occurred in one patient with malignant stricture. There was no mortality directly related to dilation in any patients.

ACHALASIA, AA Khan, Shaikh Zayed Hospital, Lahore, Pakistan

Achalasia is a motility disorder of the esophagus with the following characteristic features: loss of esophageal peristalsis, with incomplete relaxation. Ten cases of disabling symptoms of achalasia were treated with balloon dilation, reducing symptoms of regurgitation and chest pain, and with marked relief from dysphagia. Balloon dilation is safe, cheaper than surgery, and in most cases causes permanent relief.

PREVALENCE OF HBsAg and HBeAg AMONG ASYMPTOMATIC SAUDI PREGNANT MOTHERS AND HEPATITIS B VIRUS MARKERS IN THEIR FAMILIES, MA Al-Moagel, Riyadh Central Hospital

This one-year study was conducted from November 1987 to October 1988 in the main Delivery Hospitals in Riyadh. A total of 20,920 Saudi mothers were screened for hepatitis B virus infection, 14,760 of whom were categorized according to age. A follow-up screening was conducted for HBsAg-positive mothers, including all the members of their families. Seventy families (mothers, husbands, and children) were recalled and screened for hepatitis B virus markers and liver function tests. The prevalence of HBsAg among pregnant Saudi women was 3.7%, and 5.4% of these were HbeAg positive. The prevalence of HBsAg in age groups 15 to 24 and 25 to 34 years were 3.4% and 3.5%, respectively, and increased to 5% in the 35 to 45 age group. The prevalence of HBeAg was found to be lower in the older age group. There was a strong correlation between HBsAg-positive children and husbands with HBsAg-positive mothers, while all vaccinated children born to HBsAg-positive mothers were found to be HBsAg negative and anti-HBs positive, suggesting the high degree of protection given by the vaccine.

DUODENITIS IN SAUDI ARABIA: FREQUENCY AND CLINICOPATHOLOGIC PATTERN, B Ayoola, RS Al-Rashed, FZ Al-Faleh, IA Al-Mofleh, King Khalid University Hospital, Riyadh

The clinical significance of and relationship of peptic duodenitis (PD) to chronic duodenal ulcer (DU) remain controversial. To determine the frequency and clinical pattern of PD in Saudi Arabia, patients diagnosed endoscopically between 1405 and 1408H were reviewed. Of 6677 upper gastrointestinal (UGI) endoscopic examinations, 673 (10%) had PD. Of these, 402 had duodenitis only (Group A), 120 had associated peptic ulcer disease (116 DU, 4 GU) (Group B), and 169 had associated gastritis (Group C). Their ages ranged from 15 to 85 years. Positive family history for peptic disease was obtained in 9.7, 6.7, and 13.7% in Groups A, B, and C, respectively. Although the majority of patients with mild duodenitis were not treated, those treated with antacids responded fairly well. However, severe duodenitis required vigorous H_2-receptor antagonists to relieve their symptoms. Our study indicates that duodenitis may occur in three forms (Types A, B, C) and these are indistinguishable by clinical criteria. Duodenitis is a frequent cause of dyspeptic symptoms and may occasionally account for significant UGI bleeding.

ENDOSCOPIC EXTRACTION OF FOREIGN BODIES IN THE UPPER GASTROINTESTINAL TRACT: REPORT ON 61 PATIENTS TREATED AT THE ENDOSCOPY UNIT, RIYADH CENTRAL HOSPITAL 1040-1408H, MA Al-Moagel, M Al-Mofarreh, A Mohsen, A Rawashada, Y Fakunle, N Tikku, Riyadh Central Hospital

Sixty-one patients (42 M and 14 F), mean age, 20.6 years (1-80 years) and 22.2 years (1.5-60 years), respectively, had fiberoptic endoscopy because of clinical and/or radiologic evidence of foreign body ingestion. None of the patients had general anesthesia for endoscopic extraction, but a few required sedation with diazepam. Their presenting symptoms were dysphagia and retrosternal chest pain, although many were symptomless. Forty-four were treated as inpatients and seven as outpatients. The foreign bodies extracted were coins in 12; meat, bone, or food in ten; wristwatch parts in seven; needle, pin, or stapler clip in five; metal objects in four, and various other items in 14. In four patients, the foreign bodies had passed the upper GI tract at the time of endoscopy. Whenever sharp objects were being extracted, an overtube was used to protect the esophagus and hypopharynx. The sites of foreign body impact were the stomach in 29, esophagus in 22, duodenum in four, and hypopharynx in two. Endoscopic extraction was successful in 52 patients (91.2%) but failed in five (8.8%) because the foreign body was either too big or the patient was uncooperative. The foreign body impaction caused submucosal hematoma in three patients, mucosal inflammation or erosions in seven, esophageal mucosal injury in two, esophageal-tracheal fistula in one, and esophageal ulceration in one. Complications due to the endoscopic extraction were superficial mucosal lacerations in three and esophageal rupture in one.

PROSPECTIVE STUDY OF EFFECTS OF ALBENDAZOLE ON HYDATID DISEASE, MI Yasawy, MA Al-Karawi, AR El-Shiekh Mohamed, Riyadh Armed Forces Hospital

The medical treatment of hydatid disease is undergoing new developments. Until recently, mebendazole was the only active drug, but it proved to be of limited value because of its poor absorption. A new drug for *Echinococcus* (albendazole) has been introduced. Morris reported encouraging results after clinical and animal studies in which the drug was tested. A prospective study was conducted in the Gastroenterology Unit of the Riyadh Armed Forces Hospital, to evaluate the effect of albendazole for the treatment of *Echinococcus granulosus*. The study was started in May 1985. Twenty-three patients were included in the study, but one patient was subsequently excluded because of lack of proper follow-up. Mean age was 38 years; there were 11 males and 11 females. Thirty percent of the patients had a history of previous surgery with recurrence of the disease. In most of these patients, more than one surgical intervention was performed. Duration of follow-up of albendazole treatment ranged between 2 months and 3 years. The only side effect was hair loss in two patients, which was fully reversible after termination of the treatment. There was disappearance of the cysts in seven patients, a 50% reduction in cyst size in one, and 30% reduction in cyst size in three. Intracystic changes with changes in cyst appearance were observed in four patients. Rupture of the cyst occurred in two and there was no change in cyst size or appearance in two. These patients were followed-up for less than three months. It appears that albendazole is a promising treatment for this disease but further studies are needed to confirm its effectiveness.

SCHISTOSOMIAL PULMONARY HYPERTENSION, V Sivanandam, AQM Mohsen, M Khawajy, M Al-Mofarreh, Riyadh Central Hospital

The WHO has established that 200 million people are infected by schistosomiasis and another 500 million are exposed to this risk. Cardiopulmonary complications of schistosomiasis are rare and seen in only 2 to 6.5% of autopsied cases. Antemortem clinical diagnosis is rarely recorded in the literature. Pulmonary complication is due to repeated infection of *Schistosoma mansoni* or hematobium ova, leading to obliterative pulmonary arteritis and rise in pulmonary arterial pressure, right ventricular hypertrophy, and failure. Eighteen cases of severe pulmonary hypertension (PHT) of unknown cause were studied between 1406 and 1408H in Riyadh Central Hospital for a possible etiology of schistosomiasis. Bilharziasis screening included: (1) stool and urine for ova; (2) IHA for bilharziasis; (3) rectal biopsy; (4) liver biopsy; (5) GI endoscopy-duodenal biopsy; (6) cardiac catheterization in two cases. Male to female ratio was 15:3—non-Saudi, 14; Saudi's, four. The youngest patient was 18 years and oldest 47. As detailed echocardiographic evaluation ruled out congenital rheumatic heart disease, a search was made for bilharzial etiology. Sixteen of 18 patients presented with the hepatosplenic form, and this belongs to the *Schistosoma mansoni* group. Seventy percent had positive bilharzial stigmata. All presented with severe pulmonary hypertension. Duodenal biopsy was positive for bilharzial ova in 60%.

SCHISTOSOMA MANSONI FAILS TO TRIGGER RELEASE OF OXYGEN-REACTIVE METABOLITES FROM HUMAN POLYMORPHONUCLEAR LEUKOCYTES, AS Al-Tuwaijri, A Mahmoud, I Al-Mofleh, S Al-Khwaitir, AF Tawfik, College of Medicine, King Saud University, Riyadh

Stimulated human phagocyte cells increase their oxygen consumption and secretion of oxygen-reactive metabolites that are involved in microbiocidal activity and inflammation. The aim of the present study was to examine the effects of various forms of *Schistosoma mansoni* antigens, schistosomulae, soluble egg antigen (SEA), and soluble adult worm antigen (SWAB) on isolated human polymorphonuclear leukocytes (PMNS) that were oxidative burst stimulated with phorbol myristate acetate (PMA). Incubation of different numbers of schistosomulae (10-100) significantly depressed (up to 90%) the oxidative burst of stimulated PMNS as measured by a chemoluminescence (CL) technique. Different concentrations of SEA (10-100 μg/ml) induced dose-dependent inhibition of the phagocytic activity of PMNS. The potential direct cytotoxic effect of *Schistosoma* SEA on the viability of PMNS was examined at different time intervals (0-120 mins.) following incubation of PMNS with SEA. SEA has no effect on

PMNS viability as judged by the trypan blue exclusion test. The inhibitory effect of SEA is found to be reversible since PMNS pretreated with SEA and washed failed to inhibit their activity. The role of superoxide (O_2) and hydroxyl anion (OH) in the *Schistosoma*-associated inhibition of CL was studied by employment of oxygen scavengers such as superoxide dismutase (SOD), dimethyl sulfoxide (DMSO), allopurinol, or azide. The incubation of these oxygen scavengers with SEA potentiated the inhibitory effect of SEA. These results suggest (1) significant alteration of phagocytes function by interaction with schistosoma antigens, suggesting (2) similar effects in PMNS may occur during *Schistosoma mansoni* infection in humans.

VALUE OF COLONIC BIOPSY IN DIAGNOSIS OF COLONIC SCHISTOSOMIASIS, I Yasawy, MA Al-Karawi, AE Mohamed, Riyadh Armed Forces Hospital

Acute intestinal schistosomiasis usually presents with diarrhea and dysenteric-like symptoms. If not treated, complications develop that include mucosal ulcerations, polyps, granulomatous formations, fibrosis, and intestinal lumen strictures. Embolization of the ova to the liver causes periportal fibrosis and hepatosplenic schistosomiasis. Carcinoma of the rectum has been reported as a rare complication of *Schistosoma japonicum* but not of *Schistosoma mansoni* infection. This study evaluated 167 patients with schistosomal colonic disease, diagnosed by endoscopic biopsies. These patients formed part of a group of 1,775 patients with various gastrointestinal problems who had sigmoidoscopy and colonoscopy at the Riyadh Armed Forces Hospital. In the 167 patients, the colonoscopic appearance was suggestive of schistosomiasis in 86 patients (51.49%); *Schistosoma mansoni* ova were detected in stool in only 19 of these 167 patients (11.37%). The most common symptoms were abdominal pain or distention in 65 patients (38.92%). Six patients had schistosomal polyps and two had colonic tumors but no association between the tumors and *Schistosoma mansoni* infection was established. Our study of 167 patients with colonic schistosomiasis evaluated the main presentations, colonoscopic appearance, and complications. It also showed the importance and superiority of colonic biopsies in comparing stool findings and serology in diagnosing *Schistosoma mansoni* infections.

PATTERN OF ORGAN INVOLVEMENT IN SCHISTOSOMIASIS: A RETROSPECTIVE STUDY, NM Tikku, M Afzal, AB Giangreco, M Al-Mofarreh, Riyadh Central Hospital

During the period 1406-1408H, 358 patients were diagnosed as having schistosomiasis of various organs by histopathology done at the Riyadh Central Hospital. This formed about 1% of the total number of biopsies sent for histopathological analysis during this period. Eighty-eight (25%) of these patients were Saudis, of which only eight (9%) were females. Overall male to female ratio was 10:1. Mean age was 40 years (range, 2-90). The diagnosis was confirmed by identifying the schistosomal ova (calcified and/or non-seen), and an adult worm was seen in two cases. The most common organs involved were the appendix in 115 cases (32%), colorectum in 85 cases (21%), urinary tract in 82 cases (20%), and liver in 58 cases (16%). Other uncommon sites included the omentum, broad ligament, lymph node, and mesentery.

PEPTIC ULCER: EPIDEMIOLOGY AND PATHOGENESIS, IA Al-Mofleh, College of Medicine, King Saud University, Riyadh

Peptic ulcer disease (PUD) is defined as a mucosal defect in any part of the gastrointestinal tract exposed to acid and pepsin. The major forms are duodenal and gastric ulcers. PUD is worldwide in distribution but the prevalence and incidence vary considerably in different geographic locations. Marked variations may be observed within each population group. For example, it has been reported that PUD is more common in the northern compared to southern parts of Britain. Similar comparisons have been drawn between the eastern and other zones of the U.S., and between southern and northern India. PUD, especially duodenal ulcer (DU), affects males more than females in almost all populations. The ratios of male-female affectation have been reported as 4:1 and 1.5:1 for DU and gastric ulcer (GU), respectively. Duodenal ulcers are reportedly more prevalent than gastric ulcers, with a ratio of about 2-4:1 in Europe and North America. However, in developing countries, GUs are relatively less common. The DU:GU ratios have been reported to be 5:1 in India and 10:1 in Africa. In the Saudi population undergoing gastroduodenoscopy, the frequency of DU was 19% and was ten times more common than GU. The pathogenesis of PUD is not well understood. It is, however, agreed that the development of lesions occurs as a result of imbalance between aggressive factors (acid, pepsin, etc.) and defensive factors (mucosal resistance). Genetic predisposition appears to contribute, but the role of stress, alcohol, nicotine, and dietary factors in the pathogenesis of PUD is not well defined. Some drugs such as aspirin and nonsteroidal anti-inflammatory drugs are known to induce PUD and increase its morbidity and mortality. Inhibition of prostaglandin generation and enhancement of inflammatory mediators such as oxygen-free radicals, as well as platelet activating factors, have also been implicated. Recently attention has been directed at the role of *C. pylori* infection as one of the etiologic factors in PUD. Better definition and clarification of the epidemiologic characteristics and pathogenetic mechanisms of PUD are needed.

CAMPYLOBACTER PYLORI: INNOCENT OR GUILTY?, MA Laajam, King Khalid University Hospital, Riyadh

Campylobacter pylori is now established to be pathogenetically associated with active chronic gastritis. This curved, spiral microorganism can be readily detected histologically and on culture with the mucous gel, especially in the antrum, and is particularly seen in patients suffering from pyloroduodenal disease and in some with nonulcer dyspepsia. There is mounting evidence of an important pathogenic role of *C. pylori* in peptic ulcer disease. In vitro, *C. pylori* is usually sensitive to a large number of antibiotics, but there appears to be a striking discordance between in vitro sensitivity and in vivo efficacy of antibiotic therapy with respect to permanent eradication. In this regard, colloidal bismuth subcitrate alone or in combination with amoxicillin or tinizadole appears to be the most effective treatment for long-term eradication. In summary, evidence is mounting that implicates *C. pylori* as the cause of gastritis, and that shows antibacterial treatment results in normalization of gastric histology. Its relationship to peptic ulcer disease awaits further proof.

GASTROINTESTINAL REGULATORY PEPTIDES: ROLE IN PATHOPHYSIOLOGY AND DISEASE, W Creutzfeldt, University of Gottingen, West Germany

Progress in gut hormone research has not yet helped the understanding of common gastrointestinal diseases. A pathophysiologic role of gut hormones has been established only for rare conditions. This is because the clinical significance of these hormones is difficult to evaluate. Morphologic and biochemical methods used in classic endocrinology can rarely be applied to gastrointestinal endocrinology because of the special design of the gut hormone system. Also, the gut hormones and autonomic nervous system overlap in their function. A defect of one system can be compensated by the other. Gut peptides are an important link between nutrient entry and metabolism. This is realized by a hormonal gut factor (incretin) which augments glucose-induced insulin release. GIP is the most thoroughly investigated but not the only incretin. Other suggested incretin candidates are CCK and GLP-1. Until recently, of the gut peptides, only insulin and glucagon have been used therapeutically, but a long-acting analogue of somatostatin-14 has been introduced into the treatment of different gastrointestinal diseases. Several regulatory peptides stimulate or inhibit the growth of different gastrointestinal tissues in vitro and in vivo. Recently, the presence of regulatory peptides has also been demonstrated in single or sometimes even in numerous cells of gastrointestinal adenocarcinomas (so-called composite tumors). Recently, the gastrin dependency of tumor development and growth has clearly been shown for gastric carcinoids in rats and humans. Hormone receptors have been demonstrated on several gastrointestinal tumor cells. On the other hand, the available experimental literature on a growth-promoting or inhibiting effect of regulatory peptides is disturbingly contradictory. While the achlorhydria-hypergastrinemia-carcinoid sequence has contributed much to our understanding of endocrine tumor growth, a significant effect of gastrin on the growth of gastric or colon carcinomas cannot be deduced from large clinical series of patients with chronic states of hyper- or hypogastrinemia. Experimental observations have to consider such clinical experiences. Thus, there is still a long way to go until we will be able to design a complete picture of the endocrinology of gastrointestinal tumors or develop principles for their treatment with regulatory peptides.

GUT ENDOCRINOLOGY: BASIC AND CLINICAL ASPECTS, WY Chey, School of Medicine, University of Rochester, Rochester, New York, U.S.A.

There are more than 25 peptides identified in the endocrine cells of the gastrointestinal tract and pancreas. Thus, the gastrointestinal tract has the largest mass of endocrine cells and exhibits the greatest diversity of endocrine actions in the body. These peptides are relatively small in molecular size, ranging from less than 1000 daltons to about 5000 daltons. The following peptides are good examples; gastrin, a heptadecapeptide with molecular weight of about 2100 daltons; secretin, 27 amino acid residue; glucagon, 28 amino acid residue; and cholecystokinin, 33 amino acid residue. Gut endocrine cells producing a specific peptide such as secretin populate densely in the upper small intestine, whereas a relatively new peptide, peptide YY, is found in the distal small intestine and colon. The majority of these endocrine cells receive signals from the gut lumen to stimulate the secretory process of peptides. Thus, these cells reach the gut lumen with cytoplasmic processes and are called "open type" cells. On the other hand, there are basal-granulated cells that do not reach the lumen with cytoplasmic processes and are called "closed type" cells. The latter cells may secrete peptides by stimulants other than those in the gut lumen. Somatostatin-secreting cells in the gastric fundic mucosa are a good example. Secretion of peptides originating in the gastrointestinal tract occurs mostly in response to stimulants in the gut lumen. Digested products derived from food containing protein, fat, and carbohydrates, the major stimulants. They stimulate and/or control secretion of more than 10 peptides, including secretin, gastrin, and cholecystokinin (CCK). Release of certain peptides, such as motilin and pancreatic polypeptide (PP), also depends on a neural influence, in particular, a cholinergic input. For example, vagal stimulation increases the plasma level of PP and atropine blocks the cyclic increase in interdigestive plasma motilin concentration. In some cases, a gut peptide stimulates or inhibits release of another hormone (e.g., gastrin-releasing peptide stimulates the release of gastrin or secretin and somatostatin inhibits the release of gastrin). A certain hormone such as secretin is also released by pharmacologic agents including 1-phenylpentanol, licorice extract, tetraprenylacetone, and plaunotol which are derived from plants. Although release of a peptide is believed to result from direct action of a stimulant on an endocrine cell, such as L-tryptophan or oleic acid, a luminal factor other than digestive products of food or hydrochloric acid has been recently suggested to stimulate release of certain gut hormones such as CCK and secretin. Release of CCK is significantly suppressed by either pancreatic juice or trypsin. It has been suggested that a protease such as trypsin inactivates a releasing factor for CCK in the gut lumen, thereby suppressing the release of CCK. Similarly, release of secretin has also been shown to be suppressed by trypsin or pancreatic juice, and the suppression was reversed by trypsin inhibitors in the upper small intestine. Thus, the release of certain gut peptides in the circulation appears to occur as a net result of a regulatory mechanism which controls both stimulation and inhibition of peptide secretion. As peptides are released from endocrine cells, they enter the circulation (hormonal), local tissue space (paracrine), and gut lumen (luminal). Only the release of these peptides into the circulation (hormonal) and their biologic and/or physiologic actions are well known. These peptides or hormones regulate the secretory process of digestive organs, motor function of the gut, and endocrine function of the pancreas. Some regulate release of other gut hormones or peptides. Both hypersecretion and hyposecretion of certain peptides occur in various clinical conditions. Hypersecretion of a hormone is suspected when a circulating hormone level is abnormally elevated. The best known example can be found in patients with gastrinoma or Zollinger-Ellison syndrome in whom hypergastrinemia results from excessive secretion of gastrin from an islet cell tumor (apudoma) of the pancreas. Several other conditions associated with hypergastrinemia are pernicious anemia, diffuse atrophic fundi gland gastritis and achlorhydria, antral G-cell hyperplasia, retained isolated antrum, and gastric outlet obstruction. In patients with watery diarrhea syndrome (Verner-Morrison syndrome), a markedly elevated plasma level of vasoactive intestinal polypeptide (VIP) results from hypersecretion of VIP, mainly from a VIP-producing apudoma of the pancreas. Hypersecretion of pancreatic polypeptide, secretin, somatostatin, glucagon, or insulin is also found in patients with pancreatic apudomas. Hyposecretion of certain peptides is also known to occur. Secretion of both secretin and CCK is impaired in adult celiac sprue. As a result, gallbladder emptying is impaired in patients with this disease. Hyposecretion of secretin is also found in patients with achlorhydria.

GASTROINTESTINAL NEUROENDOCRINE TUMORS, W Creutzfeldt, University of Gottingen, Gottingen, West Germany

Modern immunocytochemistry has shown that functioning endocrine tumors of the gastrointestinal tract are only the tip of the iceberg. Hormone production and release by gastrointestinal endocrine tumors was first recognized in the case of an insulinoma in 1927. As late as 1953 the carcinoid syndrome has been described as a clinical entity. Carcinoids and insulinomas are still the most frequent endocrine tumors of the gastroenteropancreatic system. Other syndromes produced by gastrointestinal neuroendocrine tumors occur less frequently and are in order of prevalence: gastrinomas, vasoactive intestinal peptide (VIP) tumors, glucagonomas, and somatostatinomas. The therapeutic strategy can be summarized as follows: (1) Surgical therapy is always the first measure (complete extirpation or debulking in cases of metastasis). (2) Response to cytostatic treatment (streptozocin + 5-FU + doxorubicin) varies. Best responses occur in malignant insulinoma and VIPoma, and this should be the treatment of first choice. (3) Inhibition of hormone *secretion* is indicated until other measures are effective or have failed (diazoxide in malignant insulinoma, octreotide in all others). (4) The hormone *effect* may be counteracted by H_2-receptor antagonists or proton pump inhibitors (gastrinoma), serotonin antagonists (diarrhea in the carcinoid syndrome), and octreotide (diarrhea in VIPoma syndrome and skin lesions in glucagonoma). (5) Tumor regression and/or inhibition of tumor growth has been observed after long-term treatment with interferon-a or octreotide. Since both drugs have few side effects, further studies are justified. (6) Hepatic artery embolization is indicated if all surgical and conservative measures have failed.

PEDIATRIC ENDOSCOPY: RIYADH CENTRAL HOSPITAL EXPERIENCE, M Al-Mofarreh, Riyadh Central Hospital

"Pediatric endoscopy" is a term used to describe various endoscopic procedures in infants and children. Its use has been limited because of lack of experience and unavailability of suitable instruments. With the recent advances in the field of fiberoptic endoscopy and other experience, pediatric endoscopy is being performed increasingly. In the period of 1402-1408H (1982-1988), 557 different endoscopic procedures were performed in our hospital on patients aged from a few days to 16 years. Four hundred twenty-seven (75%) of these patients underwent esophagogastroduodenoscopy. Other diagnostic procedures, such as proctosigmoidoscopy, colonoscopy, ERCP, and laparoscopy, as well as therapeutic ones, such as polypectomies, sclerotherapy of esophageal varices, dilation of esophageal strictures, extraction of foreign bodies, and ERCP with papillotomy were performed. For upper GI endoscopy, main indications were abdominal pain, hematemesis/melena, and vomiting, while rectal bleeding and diarrhea accounted for lower GI endoscopy. The most common lesions detected were gastritis, duodenogastritis, reflux esophagitis, esophageal varices, and duodenal ulcer in the upper GI tract, and proctocolitis ulcerative colitis, and colonic polyps in the lower GI. Laparoscopy was performed for unexplained ascites, and tubercular peritonitis was detected in most.

ADVANCES IN DIAGNOSIS AND MANAGEMENT OF HYDATID DISEASE, MA Al-Karawi, AR El-Shiekh Mohamed, MI Yasawy, Riyadh Armed Forces Hospital

In Saudi Arabia, infection with *Echinococcus granulosus* is the second most important and dangerous parasitic infection after schistosomiasis. In the last decade, substantial improvement in the diagnosis and management has been achieved. In this report we reviewed our own experience and the experience of other authors in the areas of diagnosis and management. The diagnosis of hydatid disease involves the usual blood tests, including blood count, ESR, liver function tests with specific serologic and immunologic tests, and imaging procedures for detection of hydatid cyst. The Casoni intradermal test is the oldest of these tests and is now replaced by the different serologic tests, such as complement fixation test, hemagglutination test, bontonite flocculation test, and enzyme-linked immunosorbent assay (ELISA). All these tests are very useful in detecting *Echinococcus* with different sensitivity and specificity. The imaging techniques represent an important development, along with the introduction of ultrasound which can even be used in the outpatient or field conditions. CT is an additional imaging mode with promising results. It has proved to be of great help and accuracy in the investigation of liver hydatid disease and can determine size, site, and number of cysts. It is very helpful planning the surgical intervention. MRI is as helpful as CT but it does not add any more information to the ultrasound or CT findings. Both have the disadvantage of being very expensive. ERCP is also an accurate tool in diagnosing biliary *Echinococcus*. The other imaging methods, such as hepatic scintigraphy, selective angiography, plain x-ray studies, and intravenous urogram, are of secondary importance. In the management of hydatid disease there are now substantial and important developments in all aspects, whereas until now the only definite treatment for hydatid disease was surgical management. This, however, is complicated by high morbidity, mortality, and recurrence rate. The drug therapy has been positively influenced by the introduction of abendazole therapy, and most of the reports are showing positive results. In our prospective study on 22 patients using albendazole for liver hydatid cyst, patients were followed carefully with ultrasound and CT and monitoring of their serologic titers. Encouraging results were achieved in most of the patients, with disappearance of the cyst in three patients and substantial reduction of the cyst size in eight patients. In the rest of the patients there was no further enlargement of the cyst during the observation period of more than 3 years. There has also been substantial progress in the endoscopic diagnosis and management of biliary and liver *Echinococcus*. In 1985 we published the first report on the treatment of retained daughter echinococcal cysts after surgical treatment of the liver cysts, which was achieved by endoscopic sphincterotomy and evacuation of the cysts with a basket and complete clearance of the retained cysts. This method was also used by Grima, who in 1986 reported the use of ERCP and endoscopic sphincterotomy for evacuation of echinococcal daughter cysts from the biliary tree. At the same meeting, we presented the complete treatment of biliary *Echinococcus* originating from a ruptured liver cyst with evacuation of the biliary system from cysts and irrigation of the liver cyst with hypertonic saline. Complete disappearance of the main cyst without any evidence of recurrence for 1 year was achieved. With this method we have treated four additional cases. We were fully successful in three cases and only partially successful in one where we were able to evacuate the biliary tree from the daughter cyst but could not reach the main liver cyst because of blocked communication between the cyst and the biliary system. This patient then had to be referred for surgery. In the other four cases, there was no evidence of recurrence in the period of follow-up until now. Unfortunately, all other reports in the literature indicate only extraction of daughter cysts from the biliary tree, but there have been no other reports of complete treatment. A third aspect of treatment that has witnessed substantial progress is the percutaneous aspiration and drainage of hydatid cyst of the liver. Reports are now accumulating of either intended or unintended puncture of hydatid cysts, and in most patients no severe side effects have occurred. Bret et al reported 13 patients treated by this method, and the literature now indicates similar reports of unintended drainage of hydatid cysts. There are major advances in the diagnosis and treatment of hydatid disease, and with the combination of the three methods, we may now have good alternatives to surgical therapy.

INTESTINAL AND COLORECTAL SCHISTOSOMIASIS, MA Madwar, Ain Shams University, Abbassia, Cairo, Egypt

Intermittent diarrhea is probably the most common symptom of intestinal and colorectal schistosomiasis. Episodes alternate with periods of normal bowel movement or constipation, and feces often contain blood and mucus; tenesmus is also not uncommon. The abdomen may be tender on palpation, particularly along the course of the descending colon and sigmoid, and the liver may be enlarged. The main abnormal findings on sigmoidoscopy are granular appearance of the mucosa, hyperemia, exaggerated pattern, punctate hemorrhages, and tendency to bleed; ulcerations and polyps are less frequent.

PREVALENCE OF CAMPYLOBACTER PYLORI INFECTION AMONG THE SAUDI POPULATION IN RIYADH, SAUDI ARABIA, MA Al-Moagel, DG Evans, ME Abdulghani, E Adam, DJ Evans Jr, HM Malaty, PD Klein, DY Graham, Health Affairs Riyadh Region, Saudi Arabia, and Baylor College of Medicine, Houston, Texas, U.S.A.

A causative role is now accepted for *Campylobacter pylori* in type B gastritis, and evidence is accumulating that *C. pylori* infection plays a major contributory role in other diseases with which it is associated. The prevalence of *C. pylori* in any normal asymptomatic population remains unknown. We studied the prevalence of *C. pylori* infection among Saudi subjects using a specific and sensitive ELISA for IgG antibody against *C. pylori* urease. Only the first individual in the family (the index case) was used for calculation on prevalence. Subjects were interviewed and data collected about upper GI symptoms, educational level, family history, smoking, and medications. The prevalence of *C. pylori* was compared between 217 asymptomatic subjects (120 males, 97 females) and 93 with upper GI symptoms (45 males, 48 females). The ages ranged from 5 to 80 years. The data were analyzed by decade, considering that other studies have found an age-related increase in *C. pylori* infection. *C. pylori* infection was present in 28% of those below age 10. The prevalence of *C. pylori* infection in asymptomatic individuals aged 16 and older was 79%. There was no significant difference in the prevalence of *C. pylori* infection between individuals with or without upper GI symptoms. The high rate of acquisition of *C. pylori* infection precludes statistical evaluation of *C. pylori* disease associations and emphasizes that studies of *C. pylori* associations must take into account the baseline prevalence of the infection in the population.

CAMPYLOBACTER PYLORI IN SAUDI PATIENTS UNDERGOING UPPER GASTROINTESTINAL ENDOSCOPY, A Al-Quorain, HM Al-Freihi, Y Al-Gindan, EM Ibrahim, MB Satti, K Twum-Danso, H Al-Idrissi, G Al-Ghassab, A Al-Hamdan, College of Medicine and Medical Sciences, King Faisal University, Dammam

Ninety consecutive Saudi patients with abdominal pain and/or dyspeptic symptoms were recruited in a study of the prevalence of *Campylobacter pylori*. Based on endoscopic diagnosis only in the 89 evaluable patients, the isolation rates of the organisms were 73%, 83%, and 70% in normal, gastritis or gastroduodenitis, and peptic ulcer disease patients, respectively. These differences were not statistically significant. However, analysis based on histopathologic evaluation (in 73 of 89 patients) revealed contrasting results. A statistically significant difference ($P = 0.00016$) was observed between the isolation rate in histologically normal individuals (14%) and that in patients with gastritis or gastroduodenitis (89%). A similar significant difference ($P = 0.03$) was noted between the *C. pylori* detection rates in patients with gastritis or gastroduodenitis and those with peptic ulcer disease (61%). After adjustment for multiple comparisons, while the significant difference in the prevalence of *C. pylori* between normal and gastritis or gastroduodenitis patients was maintained, no significant difference was seen between gastritis or gastroduodenitis patients and those with peptic ulcer. Examination of the three methods used in detecting organisms showed gram staining, culture, and histology accurately detected *C. pylori* in 51%, 65%, and 62% of samples, respectively. The isolating capability of culture was found superior to gram staining but equivalent to histology. In vitro sensitivity testing was performed on 64 isolates.

CAMPYLOBACTER PYLORI IN SAUDIS—A PILOT STUDY, JE Beecham, H Khan, Y Shoubaki, L Hawa, King Fahad National Guard Hospital, Riyadh

Chronic gastritis, a worldwide disease affecting from 20 to 50% of the adult population, has been reported in a high proportion of Saudis attending an endoscopy clinic in Riyadh. Evidence suggesting chronic gastritis, however, has long been felt to be unsatisfactory since gastritis symptoms are often vague, frequently recur or persist despite therapy, and are not well correlated to histology. Recently, it has been suggested that *Campylobacter pylori*, a spiral gram-negative bacillus initially cultured by the Australian research team of Warren and Marshall from the mucous layer of the gastric antrum, might be the causative organism in the disease and that antibiotic therapy might, therefore, play a role in the control of chronic gastritis. However, the organism is also found in 5 to 15% of the normal population, with increased incidence in older individuals. To assess the incidence and significance of *C. pylori* in Saudis, 95 gastric biopsies taken from 88 Saudi patients attending the King Fahad Hospital Endoscopy Clinic were examined for evidence of *C. pylori* by light microscopy and culture. Histologic evidence of chronic gastritis was found in 84 of 88 individuals (95%), though suspected endoscopically in only 55%. *C. pylori* was demonstrated in 78 of these 84 patients (93%) by either histology or, less sensitively, by culture. The histologic presence of chronic gastritis correlated statistically with the presence of *C. pylori* ($P < 0.001$). The organism was found in one of four patients not demonstrating histologic chronic gastritis. This very high incidence of *C. pylori* and histologically proved gastritis did not correlate with symptoms of gastritis or endoscopic suspicion of gastritis.

CAMPYLOBACTER PYLORI IN PEPTIC DISEASE: A PRELIMINARY EXPERIENCE AMONG AN ARAB POPULATION, RS Al-Rashed, IA Al-Mofleh, B Ayoola, K Mahmoud, M Chowdury, College of Medicine, King Saud University, Riyadh

The role of *Campylobacter pylori* (CP) in patients with peptic symptoms was evaluated in 86 (57M, 29F) who underwent upper GI endoscopic examinations. Biopsies obtained from the antrum were tested for the presence of CP using the rapid urease test, microbiologic cultures, and histopathologic staining. Gastric aspirates were also tested for urease activity. Only 5 (6%) of 86 gastric aspirates showed positive urease test. The urease test was positive in 61 of the 86 (71%) biopsies from the antrum. Culture was positive in 36 of the 52 (70%) specimens cultured, and histologic staining was positive in 56 of 72 (78%) gastritis patients tested and 27 of 44 (61%) cases of CLO. For the rapid urease test, the sensitivity, specificity, and positive predictive value were 83%, 70%, and 86%, respectively. The negative predictive value was 65%. From this preliminary study, it is concluded that CP may be endemic among patients with dyspeptic symptoms in KSA and may be associated with chronic gastritis in the majority of instances. The urease test is confirmed to be an easy and effective method for CP detection.

ENDOSCOPIC MANAGEMENT OF INTRABILIARY RUPTURED HYDATID CYST, M Al-Mofarreh, MA Al-Moagel, A Al-Kraida, A Neemat, YM Fakunle, Riyadh Central Hospital

Seven patients presenting with obstructive jaundice and cholangitis due to ruptured hydatid cyst of the liver into the biliary tree were managed endoscopically. Endoscopic sphincterotomy and clearing of the biliary tract of hydatid material (daughter cysts and membranes) with a Dormia basket were followed by nasobiliary tube drainage and irrigation of the cyst cavity with hypertonic saline. In all patients, the jaundice abated and fever subsided within seven days of the procedure. On follow-up ERCP, ultrasound, and CT scans, the cyst cavity disappeared within a mean period of four weeks of the procedure. There were no immediate or long-term complications. We conclude that this procedure is preferable to surgery in the treatment of ruptured hydatid cyst into the biliary system.

ENDOSCOPIC FINDINGS IN 462 PATIENTS WITH UPPER GASTROINTESTINAL HEMORRHAGE AT KING FAHAD HOSPITAL, 1406-1409H, S Barlas, FI Khawaja, S Abu Laban, King Fahad Hospital, Medina Munawara

Endoscopic data of 462 patients with upper GI bleeding were retrospectively analyzed. There were 207 Saudis (42.6%) and 255 non-Saudis (58.4%). Age ranged from 6 to 110 years. Only 108 (21.7%) were age 60 years or above. Male to female ratio was 3.62:1, but in Saudi patients, it was 2.5:1. Esophageal varices were present in 138, among whom 36 had associated gastric varices. In 89 patients, varices were the only finding (Group I), and in 49 patients there were additional findings (Group II). The associated conditions in decreasing frequency were erosive gastritis, 26 (53%); duodenal ulcer, 16 (32.6%); gastric ulcer, nine (18.3%); duodenal erosions, five (10.2%); and esophagitis, three (61%). Deformed duodenal cap was present in two. Active bleeding from varices was noted in 25 patients in Group I. An additional 10 patients had stigmata of recent hemorrhage from the varices (blood clot in the stomach). In Group II, only three actively bleeding varices were noted. Active bleeding from the nonvariceal sources was seen in one, and five patients had evidence suggestive of recent hemorrhage from nonvariceal service. Bleeding esophageal varices remains the most common cause of admission among upper GI bleeders, both Saudis and non-Saudis. When varices was the only endoscopic finding, 27% of these patients were found to be actively bleeding and 13% had stigmata of recent hemorrhage. However, in the group of varices associated with other findings, only 6% of varices were found to be actively bleeding. Hiatal hernia, esophagitis, and MW tear were noted in much higher frequency in Saudis. The prevalence of gastric ulcer was very low—in Saudis, 3%, and in non-Saudis, 6%. Endoscopic examination was normal in 10%. The majority of these patients belonged to a younger age group (40% less than age 30). In patients age 70 or more, only 2.4% of examinations were normal. In only eight patients, no lesion was identified on first examination due to active bleeding/clot. Therapeutic intervention was done in 77 patients, heat coagulation in 15, and injection sclerotherapy in 50 patients to arrest acute bleeding. ST tube was passed in 10 patients in the endoscopy room, with resulting massive variceal bleeding.

ACUTE UPPER GASTROINTESTINAL BLEEDING IN KING KHALID UNIVERSITY HOSPITAL, RS Al-Rashed, MA Laajam, IA Mofleh, AK Al-Aska, FZ Al-Faleh, J Hussein, College of Medicine, King Saud University, Riyadh

We conducted a retrospective study, over 5 years, of all patients with a history of hematemesis and/or melena that occurred within one week of admission to KKUH who had endoscopy during the admission. Preliminary analysis of the first 86 patients is given in this abstract. Seventy-five percent of the patients were males. Saudi nationals comprised 49% and Yemeni 17% of the patients. The percentage of patients under 40 years of age was 55%. Melena alone was present in 28 patients. In 47 patients (55%), endoscopy was performed within 24 hours. The source of bleeding was identified in 52 patients (60.5%), while 27 patients had positive endoscopical findings but no bleeding source identified (16 gastric erosions, five duodenal ulcers, five esophagitis, and one stomach ulcer); and in nine patients endoscopy was normal. The major sources of bleeding identified were duodenal ulcer 42%, gastric erosions 39%, and esophageal varices 15%. Surgery was performed in five patients and sclerotherapy in seven patients; the rest were managed conservatively. There were three deaths (3.5%) in the group; in two the cause was not directly related to bleeding. From these preliminary data we conclude that peptic ulcer disease was the most common cause of bleeding and that early endoscopy may aid in diagnosing the source of bleeding. These results and conclusions are based on preliminary data.

THERAPEUTIC ENDOSCOPY AT KING FAHAD HOSPITAL, MEDINA MUNAWARA, S Barlas, FI Khawaja, King Fahad Hospital, Medina

In 3½ years, 523 therapeutic procedures of various types were performed. These include sclerotherapy of esophageal varices (150), dilation of strictures (144), endoscopic pancreaticobiliary surgery (150), coagulation of bleeding vessel (28), polypectomy (17), and foreign body removal (four). The percentage of therapeutic ERCP procedures has increased from 16 to 80% over the last 2 years. Endoscopic sphincterotomy was performed in 108 patients, including choledochoduodenostomy in 11 and pancreatic sphincterotomy in four. In 48 patients, common bile duct stones were removed and the remaining were left to pass spontaneously. Mechanical lithotripsy (six), biliary prosthesis (ten), nasobiliary drainage (11), and biliary dilation (seven) were also performed. Sclerotherapy was done as an emergency on 50 occasions, and actively bleeding varices were seen during endoscopy in 28. Dilation of esophageal strictures were performed in 129. Four patients underwent balloon dilation of pylorus, and three had pneumatic dilation for achalasia. Heat coagulation of bleeding vessels was performed using Olympus HPU, and permanent hemostasis was achieved in benign ulcer disease in 12 patients; however, only 3 of 7 postsphincterotomy bleeding problems could be controlled by this. A bleeding Mallory Weiss tear and four vascular ectasias were successfully treated. Polypectomy was performed for 12 colon polyps (11 pedunculated and a large 8 × 6 cm sessile polyp). Four esophageal polyps were removed. Massive bleeding following sclerotherapy (ten) and esophageal dilation (one) required balloon tamponade. Three episodes of postsphincterotomy bleeding were treated surgically. The use of therapeutic endoscopy is increasing rapidly. Much of the equipment needed is simple and inexpensive. For a trained endoscopist, the complication rate is very low. Newer procedures should be learned and mastered by a few in each locality and a quality control program should be put into effect.

THE ANTIULCEROGENIC ACTIVITY OF NATURAL HONEY,

ATM Mobarok Ali, MS Al-Humayyd, BR Madan, College of Medicine, King Saud University

Honey is a remarkable viscous liquid, prepared by bees from nectars of various plants. The revelation in the Holy Koran (SURA XVI, Al-NAHL; Verses 68 and 69), as well as in the Hadith, clearly describes the effectiveness of honey in a variety of diseases, including disorders of the gastrointestinal tract. However, a systematic scientific study in support of its medical attributes is lacking. In view of this, the effects of honey on indomethacin-induced gastric ulceration in rats were investigated. Oral administration of indomethacin (30 mg/kg in carboxymethyl cellulose suspension) to 72-hour-fasted rats resulted in gastric ulcers in 100%. On the contrary, there was a dose-dependent inhibition of gastric ulceration when the same dose of indomethacin was mixed with different doses of honey and administered to rats under identical conditions. Thus, there was almost 100% protection against gastric damage with the highest dose (5 g/kg) of honey used. These results suggest that natural honey has antiulcerogenic activity and may be clinically useful in preventing/reducing the occurrence of gastric ulceration if concurrently administered with potential ulcerogenic drugs. Further studies are in progress to evaluate the therapeutic usefulness of honey as well as its possible mechanism of action.

PROGNOSTIC FACTORS IN GASTRIC CANCER,

SA El-Boghdadly, KR Reynolds, King Fahad National Guard Hospital, Riyadh, and Charing Cross Hospital, London, U.K.

Records of 69 patients with gastric cancer treated at Charing Cross Hospital, U.K., for a period of 10 years were analyzed. There were 41 (59.4%) males, and 28 (40.6%) females, with a mean age of 63.4 years. The overall 5-year survival was 12.8%, which was slightly better among the curative resection group (16.3%). The mean survival of the nonresection group was 2.1 months. Among the curative resection group, the smaller the tumor (less than 4 cm) the better the prognosis (36.9 months compared to 24.3 months for tumors larger than 4 cm). The depth of penetration is important, and only five patients had early gastric cancer in our series. Lymph node involvement showed 32 months' survival for positive node compared with 33.6 months for negative node. The mean survival for poorly differentiated tumors was 38.2 months compared with 21.5 months for well differentiated. Quasi-total gastrectomy had a mean survival of 47.4, while distal gastrectomy had no postoperative mortality and a survival of 35.2 months. Total thoracoabdominal had a survival of 26 months, while total abdominal gastrectomy was 21.3 months; the former, however, carries a three times higher postoperative mortality. In conclusion, the smaller the tumor and the less the penetration, the better the prognosis. Lymph node involvement and the degree of differentiation do not alter outcome. The wider the resection the better the prognosis, but with higher postoperative mortality.

PERFORATED PEPTIC ULCER: 4 YEARS' EXPERIENCE AT RIYADH CENTRAL HOSPITAL,

A Aldhohayan, MK Alam, M Al-Mofarreh, Q Al-Qasabi, A Al-Kraida, M Al-Sebayel, King Khalid University Hospital and Riyadh Central Hospital, Riyadh

There is a marked geographic variation in the incidence of perforated peptic ulcer. This study was carried out to determine the epidemiology and management of perforated peptic ulcer in Riyadh Central Hospital. The present study was a retrospective analysis of 135 cases of peptic ulcer perforation admitted to Riyadh Central Hospital during a 4-year period. There were 130 cases of duodenal ulcer perforation and only five of gastric ulcer perforation. The majority of the patients were in their third and fourth decade; non-Saudis outnumbered Saudis. Only two women were admitted during this period. Patients were diagnosed clinically in the majority (77%) of the cases. Free gas under the diaphragm was present in 69% of the cases. All duodenal perforations were situated anteriorly. Only 33.8% of the patients were treated by definitive surgery; complications developed in 8%. There were two deaths.

THE SPECTRUM OF DIAGNOSTIC AND THERAPEUTIC ENDOSCOPIC PROCEDURES CONCERNING THE PANCREATICOBILIARY TREE AT KING FAHAD HOSPITAL, MEDINA, MUNAWARA,

FI Khawaja, King Fahad Hospital, Medina Munawara

Two hundred ninety-four consecutive ERCP and related procedures performed during the past 2$^{1}/_{2}$ years were analyzed. Only 119 patients had a simple diagnostic ERCP. Therapeutic procedure combined with ERCP was performed on 151 occasions. Twenty-four patients had a procedure not involving ERCP, e.g., peroral cholangioscopy, removal of biliary prosthesis, etc. There were 211 Saudi and only 83 non-Saudi patients, involving 150 females and 144 males. Age ranged from 16 to 90 years (average, 51.68 years), and 100 patients were age 60 years or above. Common indications were obstructive jaundice and calcular biliary tract disease (191), suspected pancreatic pathology (26), and chronic abdominal pain (18). Elective procedure for therapy was performed on 68 occasions, including 20 patients with residual common bile duct stones, where the T tube was still in place. Routine upper endoscopy was performed with the duodenoscope, and the following abnormalities were detected in 78: duodenal erosions and duodenitis (27), active duodenal ulcer (13), deformed duodenal bulb (11), esophageal and gastric abnormalities (27). The papilla was patulous (12), inflamed (four), abnormal appearing with negative biopsies (four), or carcinomatous (eight). A large suprapapillary bulge (over 1 cm) was seen in 19. A choledochoduodenal fistula occurring spontaneously was seen in seven, and due to previous endoscopic choledochoduodenostomy (four) or surgical anastomosis (two). Duodenal diverticula were seen in 38, of which 24 had some therapeutic intervention. Only one of these patients with tumor infiltrating the papilla could not be cannulated. A large fold covered the papilla in eight cases and the papilla was rolling over a duodenal fold or diverticulum in six. Failure to perform ERCP on three occasions was due to inability to locate the papilla (one), tumor infiltration (one), or submucosal intramural injection dye in the papilla (one). The last patient had a successful ERCP 5 days later. Biliary tree could not be cannulated in eight patients. A minor papilla was cannulated in one patient with pancreas divisum. Radiologic findings: ERCP was normal in 38, including 17 patients with a previous cholecystectomy. Cholelithiasis alone (47), cholelithiasis with choledocholithiasis (42), or choledocholithiasis alone (77) were the common findings. The cystic duct was blocked due to stone in 13, and 13 cases had features of Mirizzi syndrome. Biliary dyskinesia was suspected in 14. Abnormalities of intrahepatic ducts were noted in 21. Strictures of the biliary tree were seen in 14, including four with sclerosing cholangitis. Neoplasms of the pancreaticobiliary tree were seen in 32: ampullary (eight), pancreas (six), bile ducts (eight), hilum (six), and gallbladder (four). Evidence of chronic pancreatitis was noted in 19 and a pseudocyst documented in six. There were two cases of pancreatic divisum. Some form of therapeutic intervention was accomplished in 119 patients. Endoscopic sphincterotomy (ES) was performed in 108 patients. A standard ES was done in 85; however, precutting was used in eight. On 11 occasions a choledochoduodenostomy was performed and four patients had sphincterotomy of the pancreatic ductal orifice. In 48 patients, stones were removed by balloon or basket; however, in the remaining they were left to pass spontaneously. Mechanical lithotripsy was performed on six occasions. Biliary prostheses (10 or 12 F) were placed in ten and nasobiliary drainage was established in 11. Biliary dilation and/or balloon cholangioplasty was performed in seven. In conclusion, ERCP with all its therapeutic potentials has been employed in a community hospital with excellent results. Such services can be easily added at a very nominal cost if properly trained gastroenterologists are available.

EFFICACY OF SINGLE DOSE H_2 BLOCKER IN DUODENAL ULCER: COMPARISON OF CIMETIDINE AND RANITIDINE IN A DOUBLE-BLIND CONTROLLED TRIAL, IA Al-Mofleh, I Mayet, FZ Al-Faleh, RS Al-Rashed, MA Laajam, College of Medicine, King Saud University, Riyadh

To compare the relative efficacy and safety of a single dose of cimetidine (800 mg) with ranitidine (300 mg) in the short-term treatment of duodenal ulcer, 109 patients with endoscopically proved duodenal ulcer were evaluated in a double-blind randomized study. Of these, 9 female and 11 male subjects were lost to follow-up from the cimetidine and ranitidine groups, respectively. The remaining 89 patients comprised 76 males and 13 females who were between 16 and 65 years of age. The majority of our patients were Saudi (58%) and Yemeni (22%). The most common presenting symptoms prior to treatment were heartburn (63%) and abdominal pain (31%). There were a total of 31 smokers who were equally distributed in both groups. The frequency of alcohol ingestion was very low because of religious reasons and only ten patients had a history of aspirin and other nonsteroidal antiinflammatory drug ingestion. At the end of the 6-week period, 46 patients completed the course of cimetidine (Group A) while 43 patients completed the course of ranitidine (Group B). Endoscopic evaluation confirmed healing in 89% and 93% of Group A and Group B patients, respectively. Side effects were few and occurred in only four patients (two patients in each group). These were transient and mild, and consisted of headache, skin rash, and dizziness. It is concluded that a single dose of cimetidine or ranitidine given at night is efficacious in short-term healing of duodenal ulcer.

MAINTENANCE TREATMENT OF DUODENAL ULCER IN MIDDLE EASTERN POPULATION: CIMETIDINE VERSUS RANITIDINE, I Mayet, RS Al-Rashed, IA Al-Mofleh, FZ Al-Faleh, AI Al-Aska, MA Laajam, College of Medicine, King Saud University, Riyadh

A randomized prospective study is being carried out to compare single-dose cimetidine (400 mg, Group A) and ranitidine (150 mg, Group B) nocte in maintenance therapy of duodenal ulcer in a Riyadh population. Eighty-one patients with endoscopically proven duodenal ulcer were treated for 6 weeks with cimetidine (800 mg) or ranitidine (300 mg) nocte. After endoscopically proven healing of duodenal ulcer at 6 weeks, patients were followed clinically every 2 months and endoscopically at 4.5 to 12 months during the maintenance period. Side effects were monitored, as well as compliance by counting remaining medication at each visit. Twenty-nine patients in Group A and 27 patients in Group B completed the 4.5 months' follow-up. The majority of our patients were Saudis (61%) and Yemenis (23%). There were 47 males and nine females who were between 16 and 65 years of age. Ten patients from Group B were smokers. Overall, one patient from Group A and two patients from Group B had recurrent duodenal ulcers at the end of the 4.5-month follow-up. No side effects were encountered during the treatment period. It was observed that the total percentage of recurrences in our Middle Eastern population was 4.5%, and this is comparable to previous observations reported among Western populations. We observed no significant difference between the rate of relapse in either groups (Group A, 3.4%, versus Group B, 7.4%), although Group A had slightly better results. It is concluded that the single-dose therapy of H_2 blockers may prevent ulcer recurrence in the majority of patients with duodenal ulcer. Long-term follow-up is needed to establish such an advantage. These patients are currently being followed.

Poster Presentations

ANTIBODY TO LEISHMANIA DONOVANI AMONG THE SAUDI POPULATION IN MEDINA MUNAWARAH, MH Ikram, MA Qadir, King Fahad Hospital, Medina

There are two types of *Leishmania* syndromes (cutaneous and visceral) which are caused by different species of the parasite. In Saudi Arabia, cutaneous leishmaniasis is usually caused by *L. major*, while *L. donovani* is generally responsible for visceral leishmaniasis. 13,185 cases of cutaneous and 188 cases of visceral leishmaniasis were reported in 1985 to the Ministry of Health, Kingdom of Saudi Arabia. In Al Medina, 1216 people suffered from cutaneous leishmaniasis, but none contracted the visceral form. To determine the antibody prevalence to *L. donovani*, we tested 300 male blood donors and 400 pregnant women by the passive hemagglutination assay. The antibody rate among the population was 6.0%. The immune response among females (8.2%) was much higher than that in males (3.0%). The possibility exists that the infection rate due to *L. donovani* is much higher in Medina Munawarah than that suspected. Another reason could be that this response may be due to some cross-reaction between various species of *Leishmania*, because cutaneous leishmaniasis is common here.

ANTIBODY RESPONSE TO SCHISTOSOMA MANSONI AMONG THE SAUDI POPULATION IN MEDINA MUNAWARAH, MH Ikram, MA Qadir, King Fahad Hospital, Medina

Two hundred million people are infested with *Schistosoma* worldwide, and more than one million of them are in the Kingdom of Saudi Arabia. Studies have shown that the prevalence of the disease varies from 2.9 to 13% in different parts of the Kingdom. In 1983-1984, the schistosomiasis station in the Medina region reported that the rate of disease was 5.5%. The parasites identified were *S. mansoni* (3.6%) and *S. hematobium* (1.9%). In this study, feces and urine were examined microscopically for the presence of parasites and/or eggs. Because new methods have been developed to determine the immune response of the body to the antigen of the parasite, a study was conducted to find the antibody prevalence to *S. mansoni* among the healthy Saudi population. We tested samples from 300 blood donors and 400 pregnant women by passive hemagglutination assay. The antibody rate is very close to the rate found microscopically (5.1% versus 5.5%). Though the red cells were coated with antigen from *S. mansoni*, there could be some cross-reaction. Antibody rates in males are five times higher than those in females. It has been reported that the disease is more common among the younger age group, but our study was confined to adults. Therefore it can be presumed that the antibody may last for many years.

AN UNCOMMON PARASITE THAT MAY CAUSE BILIARY CIRRHOSIS: A CASE REPORT, AM Imam, MI Al-Dabbgh, King Faisal Hospital, Taif

Dicrocoelium dendriticum is a liver fluke which may uncommonly cause true biliary tract infection in man. It is believed that in rare cases it can lead to biliary cirrhosis. Spurious infections have been reported from Europe, Asia, and Africa. A recent report described six cases of spurious dicrocoeliasis from Dammam, eastern Saudi Arabia. Dicrocoeliasis is mainly an infection of the biliary tract in sheep. This communication reports a spurious *D. dendriticum* infection in a Saudi male from Taif, western Saudi Arabia. The clinician must differentiate true and spurious infections before giving treatment. It is recommended that the veterinary health authorities be sure that slaughtered animals are not infected before being sold to consumers.

PREVALENCE OF INTESTINAL PARASITES AMONG PATIENTS LIVING IN ABHA REGION, MU Khan, College of Medicine, King Saud University, Abha Branch

A retrospective study has been conducted among the patients of Shamasan Primary Health Centre to find the prevalence rates of intestinal parasites by age, sex, and seasonality. All patients whose stool samples were examined and findings properly recorded during the years 1406 and 1407H (1985-1987) have been included in the study. Results show that about 2% of the 283,622 patients underwent stool analysis. The overall parasite prevalence rate was 31.8%. All ages and sexes were affected, having higher prevalence rates in children less than 10 years of age. There were some seasonal variations in the parasite prevalence rates. The prevalence rates for *G. lamblia* was 15.5%, *E. histolytica* 7.5%, *E. coli* 6.2%, *A. lumbricoides* 1%, and *H. nana* and *Schistosoma* less than 1%. Hookworm was not seen. Although a lower prevalence rate of *Giardia lamblia* was expected, its prevalence rate in this dry and high altitude (2500-3000 meters) appears to be higher or similar to those in other parts of the Kingdom.

THE SPECTRUM OF MIRIZZI SYNDROME: A NEW CLASSIFICATION BASED ON CHOLANGIOGRAPHIC FEATURES SEEN ON ERCP, FI Khawaja, King Fahad Hospital, Medina Munawara

Impaction of gallstone in the cystic duct (CD) or in the neck of the gallbladder causing partial mechanical obstruction of the common hepatic duct (CHD) by either compression or by the resultant inflammation and chronic fibrosing reaction is known as Mirizzi syndrome. The cystic duct runs parallel to the CHD for a variable distance in such cases. A biliobilious fistula may also be present. Preoperative diagnosis may be very difficult; however, it is critical for proper surgical management. Several recent reports have described the use of PTC, sonography, or CT scan in the preoperative evaluation of Mirizzi syndrome. The role of ERCP has also been described in sporadic case reports. Lack of a standard definition and unawareness of the entire spectrum of the cholangiographic features have caused confusion and a probable underdiagnosis of this condition. In this report, cholangiographic features of 22 such patients studied by ERCP are reviewed and an attempt is made to present a classification based on these features. The proposed classification of Mirizzi syndrome is as follows: Type I: classic form: actual stenosis of CHD. Type II: variant form: stone compression of CHD from outside: IIA: cystic duct visualized (Group 1: dilated CD [lateral or medial]; Group 2: nondilated CD [lateral or medial]; IIB: cystic duct not visualized. Type III: complete retrograde obstruction of CBD/CHD junction. The distribution of the 22 cases was as follows: Type I, one case; Type II, 17 cases; Type IIA: (Group 1: 7 cases; Group 2: 7 cases); Type IIB: 3 cases; Type III, 4 cases. Eleven of the 22 patients were Saudi nationals. When the cystic duct anatomy was studied, 18% of the Saudi patients undergoing ERCP had a long cystic duct. In 90% of these cases the cystic duct entered the CHD from the medial side. Cholangiographic features of 22 patients with Mirizzi syndrome are classified according to a proposed classification. Awareness of the spectrum of findings will increase the diagnostic accuracy. The higher incidence in the Saudi population may be due to cystic duct anatomic arrangement.

USE OF INJECTION PISTOL DURING SCLEROTHERAPY FOR ESOPHAGEAL VARICES, AS Ur Rahman, FI Khawaja, S Barlas, S Abu Laban, King Fahad Hospital, Medina Munawara

Bleeding esophageal varices is the most common cause of admission among UGIT bleeders in our hospital. Endoscopic-injection sclerotherapy is used with increasing frequency both for the arrest of active bleed and elective obliteration of varices. The injection of sclerosing agent requires high pressures because of the long length of the catheter and small caliber of the injector needle. This situation is comparable to contrast injection during ERCP and consumes considerable physical strength. Toward the end of the procedure, the individual time may be prolonged due to fatigue, thus exposing the patient to a higher risk of inadvertent disengagement of the syringe from the injector, and the possibility of "sclerotherapist eye" also increases. The use of an injector pistol may circumvent these problems. Over a period of 2 years (1407/1408H), 83 patients with esophageal varices were injected with sclerosing agent using a Macron-Haber sclerotherapy needle and injector pistol (Wilson Cook). Ethanolamine oleate (5%) was injected intravariceally with a free hand technique. The injection pistol is a polycarbonate and steel device that accepts a 10 ml disposable syringe. Each trigger pull advances the injected player, forcing the syringe barrel forward. Applied leverage with spring return of the trigger makes the movement effortless and smooth. Each trigger pull is signaled by an audible click that confirms the number of injections. Individual injection volume delivered (per click) can be adjusted from 0.2 ml to 1.0%. The desired volume is injected with relative ease and rapidity. The syringe may be refilled easily through a three-way connector assembly. For purposes of sclerotherapy, each click was adjusted to deliver 0.4 ml. An injection pistol was used routinely, making sclerotherapy a short and effortless procedure. No complications related to it's use were noted. Routine use of the injection pistol is recommended during sclerotherapy. It is safe, effective, and inexpensive.

SYMPOSIUM ON PROGRESS IN THE TREATMENT OF INFERTILITY

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CLINICAL MANAGEMENT OF MALE INFERTILITY, HW Baker, University of Melbourne, Melbourne, Australia

Disorders of testicular function can contribute to infertility in up to half the couples who are seen for this problem. Disorders of spermatogenesis of poorly understood cause resulting in impaired semen quality are most common (75%). Severe disruption of spermatogenesis producing azoospermia and irreversible sterility occurs in about 13% and usually there is testicular atrophy and elevated serum follicle stimulating hormone. Definable causes such as Klinefelter's syndrome, undescended testes, and history of mumps orchitis are present in about one third of cases. Potentially treatable conditions are rare (12%) and include genital tract obstructions which may be treated surgically, gonadotropin deficiency or suppression, exposure to toxins or illness and sperm autoimmunity which may be treated medically, and coital disorders which may be treated by artificial insemination with husband's semen. Chronic nonspecific inflammation in the genital tract, nutritional disorders, and varicocele are of uncertain significance in most men with poor semen quality, and treatments for these problems usually produce no definite improvement in fertility. The place of in vitro fertilization (IVF) in the management of male infertility is being determined. Reasonable results are achieved if the semen quality is not severely impaired (> 2 million motile sperm per ejaculate), and provided there is no severe teratospermia, about 40% of oocytes are fertilized and about 10% of IVF treatment cycles result in the birth of children. With severe disorders of sperm production or morphology, fertilization rates are less than 20%, and new methods of micromanipulating sperm and oocytes are being investigated. Recently, pregnancies have been achieved with IVF using sperm collected surgically from the epididymis in men with uncorrectable genital tract obstructions. The likelihood of a subfertile couple achieving a pregnancy can be predicted from the average sperm concentration, duration of infertility, female factors, and age. Those with little or no chance of achieving pregnancy can be advised to accept this, and those with better chances can be reassured and advised to continue trying.

ROLE OF ULTRASOUND IN THE WORK-UP OF INFERTILITY, C Hamilton, King Faisal Specialist Hospital and Research Centre, Riyadh

Because it can visualize the ovarian activity noninvasively, diagnostic ultrasound is an ideal tool to monitor the menstrual cycle. It is more reliable in detecting the exact moment of ovulation than the basal body temperature chart, and therefore ultrasound is now used to screen new infertility patients. Starting on cycle day 10, serial scans are made until the graafian follicle ruptures. As soon as the dominant follicle is 16 mm in diameter, the patient is instructed to have regular intercourse and then a postcoital test (PCT) is performed. If the test is negative and the follicle is still present two days later, the PCT is repeated. If necessary, mucus can be collected for a sperm-mucus penetration test or anti-sperm-antibody assay later on in the cycle. Seven days after ovulation, a progesterone sample is taken. As soon as the period starts, the duration of the luteal phase is calculated. This fertility screening cycle (FSC) appears to be more reliable and efficient than the traditional way of screening. A higher specificity of tests prevented unnecessary repetition of investigations. By applying the FSC, we were able to reduce the duration of the basal screening to only one fourth of the usual time needed. Furthermore, ovulation disturbances could be detected at an earlier stage. We believe that ultrasound, aside from its role in infertility treatments (like ovulation induction, timing of insemination, and in vitro fertilization), also plays an important role in the work-up of infertility.

EXTRASELLAR PROLACTINOMAS: MEDICAL MANAGEMENT WITH BROMOCRIPTINE, E Al-Dossary, NJY Woodhouse, King Faisal Specialist Hospital and Research Centre, Riyadh

Forty patients (20 males, 20 females) with an extrasellar prolactin-secreting tumor and mean prolactin level greater than 4000 (normal, 0-21) μg/mL received bromocriptine for 13 to 400 weeks. Normal or near normal prolactin levels were achieved in more than 90% of the patients, and this was accompanied by CT scan evidence of tumor shrinkage in all but two patients. Visual abnormalities improved rapidly in 10 of 16 affected patients, including one whose tumor did not shrink after 12 weeks of treatment although his prolactin levels were normal. So far, seven of the 20 females have conceived—five after bromocriptine alone and two after ovulation induction as well. After stopping bromocriptine, tumor regrowth occurred in all but one patient whose prolactin levels remained normal during two pregnancies. There were no complications. Bromocriptine may safely be used to restore fertility in patients with large extrasellar tumors. Careful monitoring is essential if treatment is withdrawn during pregnancy.

IMMUNE ASPECTS OF INFERTILITY: SIGNS OF AUTOIMMUNE ABERRATION IN HEALTHY WOMEN WITH UNEXPLAINED RECURRENT ABORTION, AM Unander, R Norberg, H Wennerstrom, M Haeger, L Arfors, L Stigendal, Sahlgren Hospital, and National Bacteriological Laboratory, Sweden

Four hundred fifty couples with unexplained recurrent abortion were investigated. The women had had three or more (mean, 4.7) abortions each, and all were healthy. None had a primary diagnosis of systemic lupus erythematosus (SLE). The women's sera were investigated for blocking antibodies in one-way mixed lymphocyte culture, anticardiolipin antibodies (ACA), antinuclear antibodies, and anti-DNA. Plasma samples were tested for activated partial thromboplastin time (APTT) and complement factors C3 and C4. A control group of 136 normal pregnant women was investigated for ACA in repeated blood samples drawn during pregnancy. Eighty-five percent of the women with habitual abortion lacked blocking antibody, whereas 15% had strong blocking antibody. ACA levels were normal (0-2 units) in 78% of the women. Raised levels of ACA were found in as many as 22% of healthy women (> 10 units in 6%). Of 136 pregnant women, 11 (8%) had demonstrable ACA at any time during pregnancy. ACA could be demonstrated at all four sampling occasions in three women (2%), one of whom (1%) had > 10 units. The habitually aborting woman with high ACA values had significantly lowered levels of C4, demonstrable antinuclear antibodies, and immune complexes, but C3 levels were normal. Contrary to what has been claimed, the pattern of early pregnancy loss did not discriminate between the autoimmune cause and other types of recurrent abortion. The mean values of APTT were higher in women with raised levels of ACA, although only those with ACA levels of > 10 units displayed pathologically raised APTT values. Fifteen women with raised ACA levels (3 with > 10 units) lacked blocking antibody, received leukocyte transfusions, and then had infants without any treatment with prednisolone or aspirin. A raised ACA value alone is not enough cause for treatment with prednisolone and aspirin during pregnancy. Only habitually aborting women who display ACA levels concomitant with strong blocking antibody, low levels of C4, and high APTT values should receive prednisolone and aspirin. Those women seem to have an autoimmune entity of recurrent abortion and raised ACA, possibly with other signs of autoimmune aberration but without any symptoms of autoimmunity other than miscarriages. They may be at a high risk of developing SLE and therefore should be surveyed regarding the development of SLE symptoms.

SPERM AUTOIMMUNITY, HW Gordon Baker, University of Melbourne, Melbourne, Australia

Sperm autoimmunity is found in approximately 5% of men being investigated for male infertility. In some, the sperm autoimmunity is associated with genital tract obstruction. Sperm may be absorbed into the systemic circulation, a cause of the obstruction, and lead to immunization. In other patients who have sperm antibodies but no clear immunizing event, there are frequent family histories of autoimmune diseases, particularly of the thyroid and parietal cells (pernicious anemia). Such patients have a higher frequency of organ-specific autoantibodies in their sera than do sperm-antibody-negative controls. Rare patients are seen with autoimmune orchitis with inflammation in one testis. It has been suggested that removal of the affected testis may result in cure. Screening patients for sperm autoimmunity involves detection of antibody coating on sperm directly by the immunobead test, or measurement of sperm antibody activity in serum or seminal plasma by sperm agglutination and immobilization or indirect immunobead tests. New methods of measuring sperm antibodies with specific immunoglobulin-binding proteins are being developed. Techniques based on immunofluorescence or enzyme-linked immunosorption methods with fixed sperm are unacceptable, as results do not correlate with standard tests. As up to 1% of fertile men have sperm antibodies, a sperm/cervical mucus interaction (Kremer test) is used to check the significance of all positive tests and could also be used as a screening test. Severe sperm autoimmunity is characterized by an inability of sperm to penetrate through cervical mucus (< 2 cm in 1 hour). About 85% of men found to have sperm antibodies by immunobead test have failure of sperm/cervical mucus penetration. These patients have a bad prognosis if the condition is untreated—the pregnancy rate is < 0.5% per month. Treatment with high-dose prednisolone will increase the pregnancy rates to about 5% per month. Methods of administration of prednisolone include continuous high-dose (50 mg per day for 4-6 months) or intermittent regimens. Side effects may be less with intermittent therapy. Other methods of immunosuppression, such as cyclosporin, have not been investigated in controlled trials. Artificial insemination and in vitro fertilization may be carried out using sperm cryopreserved during prednisolone treatment. In the future it is hoped that the antigens involved in sperm autoimmunity will be identified and the mechanisms by which sperm antibodies interfere with fertilization discovered. It may then be possible to remove or block the antifertility effects without resorting to immunosuppressive therapy.

OVULATION INDUCTION: NEW DEVELOPMENTS, RW Shaw, The Royal Free Hospital, London, England

There have been a number of advances in the field of ovulation induction within the last decade. A most significant one has been the introduction of pulsatile luteinizing hormone releasing hormone (LHRH) therapy in appropriately selected cases. Two other specific developments have occurred in more recent years. These have been related to the use of purified preparations of gonadotropins, essentially pure follicle stimulating hormone (FSH) preparations, and the development of protocols utilizing pituitary desensitization with LHRH analogues prior to ovulation induction therapy. Induction of ovulation in women with hypogonadotropic hypogonadism using human menopausal gonadotropin (hMG) has been performed successfully for many years. With appropriate monitoring, high pregnancy rate and low complication rate can be achieved. However, when there is increasing functional pituitary capacity, the incidence of complications in hMG therapy increases and the pregnancy rate decreases. Hyperstimulation is usually the response to human chorionic gonadotropin (hCG) administration and, as such, does not interfere with the process of ovulation itself, but merely complicates the likelihood of implantation and pregnancy continuation. Premature luteinization/ovulation, however, is caused by a surge or rise of luteinizing hormone (LH), which occurs in response to increasing circulating estradiol levels prior to the criteria for administration of the ovulatory dose of hCG being satisfied. This pre-hCG luteinization probably has adverse effects at both the ovarian and endometrial levels. Those women who are particularly prone to this problem are those with polycystic ovary (PCO) syndrome. Administration of an LHRH analogue over a period of 10 to 14 days will desensitize the pituitary, suppress endogenous circulating LH and FSH levels, and prevent pulsatile release. In addition, continued administration of the LHRH analogue in conjunction with administration of exogenous gonadotropins leads to follicular stimulation. Continuation of the LHRH analogue until the full criteria for hCG administration have been achieved prevents premature luteinization. This results in the majority of cycles reaching ovulation without problem. Patients with PCO syndrome are those in whom purified FSH preparations have also been utilized in recent years to overcome basic endocrinologic disorders relating to elevated levels of endogenous LH. The results from using purified FSH preparations are now accruing, suggesting that they do have advantages in certain patients, though they are not necessarily the solution for all problems associated with induction of ovulation in PCO syndrome.

ULTRASONOGRAPHIC AND HORMONAL FINDINGS IN FOUR GROUPS OF PATIENTS TREATED WITH HMG/HCG, N Agarwal, UV Sieck, C Hamilton, King Faisal Specialist Hospital and Research Centre, Riyadh

Ovarian response was studied in 179 cycles of 123 patients who underwent ovulation induction with human menopausal gonadotropin and human chorionic gonadotropin (hMG/hCG) in the infertility clinic of a tertiary care hospital in Saudi Arabia. The patients could be categorized into four groups: (1) hypogonadotropic amenorrhea (35 cycles), (2) polycystic ovarian disease (PCOD) (66 cycles), (3) dysmucorrhea (35 cycles), and (4) hyperfertilization because of male factor (43 cycles). Patients were monitored by serial ultrasound, and for daily luteinizing hormone and estradiol (E2) levels. Not only the diameters of the dominant follicles were measured by ultrasound, but also the number of follicles larger than 10 mm and the size of the ovaries on the day of hCG administration. One week later, serum progesterone level and ovarian size were measured again. Hyperstimulation was found more often in the PCOD group than in others. Good correlations were found between the maximum E2 level and the number of follicles above 10 mm on the one hand and the midluteal ovarian size on the other. The size of the dominant follicle and the size of the ovaries on the day of hCG administration correlated less with the midluteal ovarian size. There was no case of severe hyperstimulation. The pregnancy rate per cycle was similar in hypogonadotropic amenorrhea (15%), PCOD (14%), and dysmucorrhea (14.8%), but was only 8% per cycle in the group with male infertility. hMG stimulation can safely be monitored by a combination of serial E2 measurement and ultrasound. The degree of hyperstimulation can be predicted and severe hyperstimulation can be prevented.

AN ATTEMPT TO CONQUER THE ENIGMA OF PCOS USING DIFFERENT MEDICAL REGIMENS INCLUDING GnRH ANALOGUE, M Awad, TO Sabagh, Armed Forces Hospital, Riyadh

We conducted a randomized group study on patients with polycystic ovarian syndrome (PCOS) attending the infertility clinic at the Riyadh Armed Forces Hospital between 1986 and 1988. The total number of patients seen was 280, and of these, 70 had PCOS. The criteria for diagnosing this syndrome were based on either clinical, biochemical, or histologic findings. Ultrasonography was not used to diagnose the morphology of the ovaries. In addition to the usual regimens used for this condition (clomiphene citrate and gonadotropins), bromocriptine, prednisolone, and gonadotropic releasing hormone analogue were used. Most of the patients underwent laparoscopy and bilateral cautery to the ovaries. Following ovarian cautery and the start of the triple regimen, all amenorrheic patients started to have normal menses. Thirty (42%) of the patients in our study got pregnant following the regimen.

HYPOTHALAMIC HYPOGONADISM–CLINICAL FEATURES AND RESULTS OF TREATMENT, O Odugbesan, NJY Woodhouse, King Faisal Specialist Hospital and Research Centre, Riyadh

More than 60 patients with hypothalamic/hypogonadism due to presumed gonadotropin releasing hormone (GnRH) deficiency have been seen in the KFSH endocrine unit since 1980. The diagnosis was established by history and physical examination, together with basal testosterone/estradiol and luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels. GnRH studies were carried out in most patients and clomiphene citrate testing in half. Treatment with sex hormone replacement was started in all patients, and if fertility was desired, patients received either injections of Pergonal (FSH) and human chorionic gonadotrophin (LH), or pulsatile subcutaneous injections of GnRH (20%). In women, ovulation occurred in almost every patient, regardless of treatment. In men, however, spermatogenesis occurred in only 50% of the patients, in spite of correcting the endocrine deficit. A most important factor regarding fertility prognosis in the male is pretreatment testicular size.

RATIONALE AND USE OF LHRH AGONISTS IN ENDOMETRIOSIS, RW Shaw, Royal Free Hospital, London, England

Endometriosis is a difficult disease to treat, as often response to therapy relies on recognition of the disease in its earliest possible stages. Recurrence eventually occurs in up to 60% of cases following most treatment modalities. Ectopic endometrial tissue does respond to endogenous and exogenous ovarian sex steroid hormones in a fashion sufficiently similar to that of normal endometrium to suggest that a hormonal approach altering circulating estrogen and progesterone levels is beneficial. Hypoestrogenic states particularly induce atrophy and regression of endometriotic deposits. Continued administration of luteinizing hormone releasing hormone (LHRH) analogues produces a "medical oophorectomy" and hence is ideal for treating endometriosis. Initially, small, uncontrolled studies demonstrated the efficacy of LHRH analogues in the treatment of endometriosis. A number of open randomized controlled comparative and double-blind comparative trials of LHRH analogues against Danol have now been undertaken. These demonstrate significant and sustained improvement in the symptoms of endometriosis patients and marked resolution of the deposits at laparoscopic assessment, even in extensive and severe cases. Deep-seated endometriotic deposits, particularly those within the ovary, respond less well and are more likely to recur following medical treatment.

TRANSVAGINAL ULTRASOUND-GUIDED OOCYTE RETRIEVAL: A REVIEW OF 750 PROCEDURES, UV Sieck, JLH Evers, GG Gnany, C Hamilton, JF Larsen, C Sherwood, KV Sheth, King Faisal Specialist Hospital and Research Centre, Riyadh

Since the start of the in vitro fertilization (IVF) program at King Faisal Specialist Hospital and Research Centre in October 1986, 750 procedures have been performed in 435 patients. From the first oocyte retrieval onward, all procedures were carried out by a transvaginal ultrasound-guided technique. No major complications occurred. In 1.9% of the procedures, vaginal bleeding required swab pressure, while in only 0.1% the ovum pick-up had to be discontinued because of active bleeding. The standard dosage of sedation/analgesia used was 50 mg meperidine IV and 10 mg of diazepam IV. More than 95% of the patients tolerated the procedure well or excellently. A mean yield of 4.2 oocytes was obtained. Over time the oocyte recovery rate increased from 40 to 90%, while the mean duration of the procedure decreased from 30 to 6 minutes. Transvaginal ultrasound-guided follicle aspiration for IVF is a simple and safe procedure. It can be learned rapidly and tolerated well by the patient.

ENDOCRINOLOGIC AND ANDROLOGIC ASPECTS OF IVF IN SAUDI ARABIA, C Hamilton, JLH Evers, GG Gnany, K Jaroudi, JF Larsen, C Sherwood, KV Sheth, UV Sieck, King Faisal Specialist Hospital and Research Centre, Riyadh

From the start of the in vitro fertilization (IVF) program at KFSH&RC it was clear that a considerable number of patients showed an abnormal hormonal response to the standard induction protocols. These patients either had a relatively high follicle stimulating hormone (FSH) level and needed a high dose of gonadotropins (premature menopausal pattern) or had a high luteinizing hormone (LH)/FSH ratio, indicating polycystic ovarian disease (PCOD). This is not surprising if we realize that the average weight and height are 70 kg and 1.55 m, respectively, while in a university hospital these figures were 65 kg and 1.62 m, respectively. Forty-three percent of the cycles stimulated with human menopausal gonadotropins (hMG) alone, a combination of clomiphene and hMG, or a combination of FSH and hMG showed premature luteinization, accompanied by a low pregnancy rate. Since Buserelin (an LHRH analogue) was added to the standard induction protocol, the success rate has increased. In our patient population, the long Buserelin scheme, in which the Buserelin is started in the previous cycle, gives better results than the short Buserelin scheme, in which Buserelin is started on cycle day 2 of the treatment cycle. Because most of the PCOD patients are anovular, we start the long Buserelin scheme on day 15 of a cycle with oral contraceptives. Another factor that precludes comparison of our results with other IVF centres is the extremely high percentage of male infertility (29%). In countries where alternative solutions for male infertility exist, the percentage usually is around or below 5%. Of all the sperm parameters, sperm motility after the swim-up test correlated best with the fertilization rate and pregnancy rate. No pregnancy was obtained if sperm motility was less than 20% before the swim-up test and/or less than 40% after the swim-up test.

ELECTROMICROSURGERY, SWOLIN TECHNIQUE IN GYNECOLOGY, K Swolin, University of Goteborg, Goteborg, Sweden

The different applications of electromicrosurgery for treatment of female infertility are demonstrated in 4 patients, including postoperative laparoscopy. I conceived and developed this technique in the 1950s and then in 1960 introduced its practical application at the Department of Obstetrics and Gynecology at the University of Goteborg. The method and initial short-term results were part of a thesis on the surgical treatment of female sterility which was published in 1967 with subsequent reprints in 1968 and 1981. In principle, all types of interventions for infertility can be performed with this technique, e.g., lysis of adhesions (from uterus, tube, ovary, omentum, and peritoneum) and the three main types of tubal plastic surgery: anastomosis, implantation, and salpingostomy. This special and atraumatic technique is not only suitable for the surgical management of female and even male sterility, it should be used—eventually without magnifying devices—for all surgical interventions in the small pelvis of young women who have not been able to complete childbearing. Simple minor interventions such as resection of an ovary can lead to about 50% involuntary sterility because of postoperative adhesions. This technique is suitable even for general abdominal surgery for otherwise problematic postoperative adhesions. Apart from the cutaneous incision which is made by a scalpel, all the remainder of the operation is performed by means of microelectrodes. Contrary to the conventional technique, the surgeon, using as much time as needed, works as atraumatically and as bloodlessly as possible to avoid postoperative adhesions. For this work—beside magnification using loupes and microscope—microelectrodes, Teflon rods, and fingers are regarded as essential instruments.

SIGNIFICANCE OF INTRAUTERINE ADHESIONS DETECTED HYSTEROSCOPICALLY IN EUMENORRHEIC INFERTILE WOMEN AND ROLE OF CURETTAGE IN THEIR FORMATION, PJ Hill, King Fahad National Guard Hospital, Riyadh

Increasing use of hysteroscopy in diagnosing the cause of infertility has shown that intrauterine adhesions are of greater concern, especially in eumenorrheic women, than was previously recognized. Their significance is not yet completely clear. We compared the incidence of such lesions detected hysteroscopically in 242 women with otherwise unexplained infertility with their incidence in a group of 33 potentially fertile women. The outcome after treatment was recorded. The effect of curettage on the potential production of these adhesions was examined. The incidence of adhesions in the infertile group was considerably greater than that in the fertile group. A 50% pregnancy rate was observed following lysis of the adhesions. An antecedent history of curettage was associated with a significantly higher incidence of adhesion formation than that found in noncuretted patients.

CHLAMYDIAL INFECTION IN SAUDI INFERTILE PATIENTS, HSO Abduljabbar, HA Mosli, FS Gazzaz, King Abdulaziz University Hospital, Jeddah

In the infertility and andrology clinics at King Abdulaziz University Hospital, Jeddah, we tested 65 specimens from 31 female and 34 male patients. The male patients were suspected of having chlamydial infection. All 31 female patients had laparoscopy for evaluation of the tubal factor. A direct test using fluorescein-labeled monoclonal antibodies was used for the identification of chlamydial elementary bodies in direct smears taken from the endocervix in female patients and the urethra in male patients; 29% (9/31) and 26% (9/34), were positive in the endocervical and urethral specimens, respectively. We compared the results of laparoscopy findings in the nine patients positive for chlamydial infection with the 22 patients negative for infection and found 7/9 and 6/22 patients had tubal disease ($P < 0.05$).

EFFECTS OF CAFFEINE AND DEOXYADENOSINE ON HUMAN SPERM MOTILITY, HP Baer, E DeVol, C Hamilton, A Moorji, KV Sheth, NJY Woodhouse, King Faisal Specialist Hospital and Research Centre, Riyadh

We have investigated the effects of caffeine (C) and deoxyadenosine (D) on human sperm motility parameters, using normal and submotile human sperm, in order to probe their potential for therapy of normal and submotile human sperm, to probe their potential for therapy of submotile and subfertile sperm. Parameters were measured by an automated analyzer (CellSoft system; Cryo Resources, NY). C (7 mM) and D (3 mM) increased motility of washed sperm about twofold; this was more pronounced in specimens with low initial motility. The maximal degree of stimulation was reached within less than 30 min and persisted for at least 4-6 h. However, after 24 h (37°C, 5% CO_2, Ham's F medium with 5 mg/mL bovine serum or 15% human cord serum), increased motility remained only in about 50% of specimens. None of the other motility parameters (velocity, beat frequency, lateral head displacement) seemed affected by the drugs. Combination of C and D did not result in additive or synergistic stimulation of motility. In a further series of experiments, the effects of C and D on the yield and motility of swim-up sperm were measured. Both drugs increased the yield of swim-up sperm by about 1.5- to 2-fold, and sperm thus selected also showed significantly enchanced motility (1.5-fold) compared to controls. Our studies suggest that motility enhancement by C or D occurs over periods compatible with routine in vitro fertilization (IVF) requirements. As well, the use of the drugs in swim-up selection of sperm is promising, since in our experience carryover of the drug from the original incubation to the preparations used in IVF is minimal. To date we have not investigated whether C or D also increase the IVF potential of submotile sperm.

MALE INFERTILITY–155 CONSECUTIVE CASES, A Jamal, MS Abomelha, K El-Otaibi, Riyadh Armed Forces Hospital

We studied the experience and results of treatment in the first 155 consecutive male infertility patients seen during 1981-1983 at the Riyadh Armed Forces Hospital. There was a high incidence (46%) of primary testicular failure of unexplained etiology as well as idiopathic oligospermia (27%) and obstructive azoospermia (27%). Abnormalities shown by the semen analysis were more profound than those seen in the West, and a significant number of infertility cases were due to a male factor alone. The clear relationship between absent spermatogenesis on testicular biopsy and raised levels of follicle stimulating hormone is confirmed. Scrotal varicoceles were associated with profound testicular changes on histology, and therefore varicocele surgery did not improve the chances of pregnancy, as reported in the West.

SEMEN ANALYSIS AND NEW TESTS OF SPERM FUNCTION, HW Gordon Baker, The Royal Women's Hospital, Melbourne, Australia

Semen analysis involving measurement of sperm concentration, motility, and morphology remains the most important investigation for assessment of fertility in men. However, it is a poor guide to potential fertility except when there is an absolute abnormality, such as persistent azoospermia or zero sperm motility. While currently unquantifiable variations in female fertility are probably mainly responsible for the poor relationship between semen quality and fertility, the existence of technical errors and the biologic variability of sperm output also contribute. Laboratory errors can be minimized by careful training of technicians and should be monitored by a quality control program. The introduction of automated methods for cell counting, motility, and morphology assessments have been predicted to improve the objectivity of assessment. However, the currently available systems suffer from poor reproducibility and interference from debris in the semen, especially when sperm concentrations are low. Biologic variation in semen analysis results is related to problems of collection of semen, intercurrent illness, and sometimes environmental factors such as temperature. Some disorders of semen quality may also fluctuate in severity, such as sperm autoimmunity and necrospermia. Adequate statistical methods for relating multiple semen analysis variables to fertility have only been developed recently. Cox regression analysis of pregnancy rates in about 1300 subfertile couples showed that sperm concentration was the most significant factor related to fertility, and additional factors such as sperm motility and morphology were not independently significant once sperm concentration was taken into account. However, we found sperm donors with high pregnancy rates (> 15% per cycles) had better sperm morphology than those with lower pregnancy rates (< 5% per cycle), and recently we have also found a very strong relationship between sperm morphology and human fertilization rates in vitro. In vitro fertilization (IVF) has provided a new method for assessing some aspects of the potential fertility of sperm. In addition to sperm morphology, we have found that the ability of sperm to bind to the zona pellucida of oocytes that have failed to fertilize in vitro and the proportion of sperm with normal intact acrosomes in men with poor morphology are also additional significant predictors of IVF results. However, other tests such as hypoosmotic swelling, stains for nuclear immaturity, sperm head decondensation in detergents, and measurements of acrosin levels were not significant.

IMMUNOTHERAPY EXPERIENCE WITH MULTIPLE ABORTION CASES AT KING FAISAL SPECIALIST HOSPITAL AND RESEARCH CENTRE, KV Sheth, C Hamilton, UV Sieck, King Faisal Specialist Hospital and Research Centre, Riyadh

Thirty-nine patients who had had three or more first-trimester abortions were investigated for the presence of cytotoxic antibody and also had chromosomal analysis. Patients with negative cytotoxic antibody and normal karyotype underwent immunotherapy using separated lymphocyte transfusions of the husband's blood given during the first eight weeks of gestation. The immunotherapy was repeated every 12 weeks. No adverse reactions to transfusion were observed in any of the treated patients. A total of 21/39 (54%) of the patients treated delivered full-term normal infants. Our success rate is lower than that reported elsewhere (60-80%). This can be explained by the recent demonstration of blocking factor in the sera of 23 of 55 (41%) patients who were cytotoxic antibody-negative and had had multiple abortions. The presence of blocking factor in sera contraindicates immunotherapy. No blocking factor test was performed in our 39 patients.

SURGICAL THERAPY FOR MALE-FACTOR INFERTILITY: IS IT WORTH IT? MM El-Gammal, King Faisal Specialist Hospital and Research Centre, Riyadh

Identifiable correctable causes of male factor infertility are few when compared with the incidence of idiopathic infertility. Moreover, the results of surgical treatment are not encouraging. Over a period of two years, 96 infertile male patients were referred to the Urology Section at King Faisal Specialist Hospital regarding possible correctable surgical causes. Seventy-six patients were azoospermic (77%), 12 had oligospermia (13%), and eight presented with ejaculatory dysfunction (four retrograde ejaculation, two ejaculatory failure, and two ejaculatory duct obstruction). In the azoospermic group, vasoepididymostomy was the most common treatment. Fifty-four patients underwent this procedure with different techniques, and only one patient had reappearance of sperm in the ejaculate. For the oligoasthenospermia group, retroperitoneal repair of varicocele was performed in nine patients without significant improvement in the spermogram parameters. Similar poor results were obtained in the ejaculatory dysfunction group. Only two retrograde ejaculators responded to alpha-stimulant medications, while operative sperm collection and subsequent in vitro fertilization were unsuccessful in two patients with ejaculatory failure. Faced with these poor results, we recommend re-evaluation of the patient selection process, as well as of the indications and techniques of surgical treatment for male factor infertility.

IMMUNE INVESTIGATION OF HABITUAL ABORTION: 85% LACK BLOCKING ANTIBODY, 5% HAVE AUTOIMMUNE ABERRATION, 10% REMAIN UNEXPLAINED. SUCCESS FOR IMMUNIZATION BY THIRD PARTY LEUKOCYTES IS PREDICTED BY THE PRODUCTION OF PREVIOUSLY ABSENT BLOCKING ANTIBODY, AM Unander, C Slosteen, A Lindholm, A Enskog, D Robbins, T Soderstrom, Sahlgren Hospital, Goteborg, Sweden

Four hundred fifty couples with unexplained recurrent abortion were investigated. The women had had three or more (mean, 4.7) abortions each and all patients were healthy. No explanation for the abortions had been found. The women were studied concerning cellular immune responses and blocking antibodies in one way mixed lymphocytic culture (MLC). Serum specimens were tested for anticardiolipin antibodies and plasma specimens for activated partial thromboplastin time. Each of 280 women received three or five leukocyte-rich erythrocyte concentrates from different third-party donors. The specificity of antibodies before and after transfusion was investigated using flow cytometry. Eighty-five percent of the women with habitual abortion lacked blocking antibody, whereas 15% had strong blocking antibody. The postimmunization abortion rate was below 10% among women who had lacked blocking antibody before the transfusions compared to 94% among those who had blocking antibody. Pregnancy results were therefore not improved by transfusions in women who had blocking antibody before treatment, irrespective of their autoimmune status. After immunization, pregnancies were uneventful, and the infants were healthy. There was no increased frequency of intrauterine growth retardation or malformations. The induction of previously absent blocking antibody in one-way MLC is a prognostic sign of success for immunization treatment of recurrent abortion. The formation of antibody against CD4-positive husband lymphocytes is parallel to the development of blocking antibody and of the same prognostic value. No increased frequency of pregnancy complications is found after immunization using third-party leukocytes.

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Riyadh, Saudi Arabia

Announcements

The *Annals of Saudi Medicine* is pleased to publish announcements of educational opportunities of interest to its readers. For adequate publicity, notices of postgraduate courses, meetings, and lectures must be received at least 6 months before the date of occurrence. Please send relevant information to the *Annals of Saudi Medicine*, Publications Office, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia.

King Saud University Hospitals Postgraduate Training Programs

King Saud University Hospitals (King Khalid University Hospital/King Abdul Aziz University Hospital) are pleased to invite applications for the following postgraduate training programs:

1. Arab Board residency training in the specialties of internal medicine, pediatrics, surgery, and obstetrics/gynecology.
2. Diploma courses in medical radiodiagnosis, laryngology/otology, psychiatry, and family practice.
3. Master's degree courses in pathology and family practice.
4. Residency training program in ophthalmology (in conjunction with King Khaled Eye Specialist Hospital).

For further information, contact the Director, Postgraduate Medical Education, College of Medicine, King Saud University, P. O. Box 2925, Riyadh 11451, Saudi Arabia.

King Faisal Specialist Hospital and Research Centre Postgraduate Training Programs

King Faisal Specialist Hospital and Research Centre is pleased to invite applications for the following full-time postgraduate training programs:

1. Arab Board residency training in the specialties of internal medicine, obstetrics/gynecology, pediatrics, and surgery.
2. Five-year pathology residency training program, affiliated with the Royal College of Pathologists of Australasia and the King Saud University.
3. Fellowships in cardiology (adult and pediatric), endocrinology, gastroenterology, infectious diseases, nephrology, and oncology (adult and pediatric).

For further information contact the Director, Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia; telephone (01) 464-7272, extension 1837.

King Saud University Fellowship in Pathology

King Saud University announces the inception of a 5-year joint fellowship training program in pathology. The training will be at King Khalid University Hospital, King Faisal Specialist Hospital and Research Centre, and Riyadh Armed Forces Hospital, and is a full-time program. Application is open to interested and suitably qualified residents from all over the Kingdom. To be eligible, applicants will meet the following criteria:

1. Doctors who hold MB,BS from King Saud University or equivalent degree with at least Good grade.
2. Doctors who have finished their internship in a recognized hospital with at least a Very Good grade.
3. Successful completion of a selection examination and personal interview.
4. Applicants from other institutions should submit a letter from his/her employer that he/she will be sponsored during the whole period of training.

Applications and inquiries should be sent to the Director, Postgraduate Medical Education, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia.

Radiopharmaceuticals from King Faisal Specialist Hospital and Research Centre

King Faisal Specialist Hospital and Research Centre manufactures various radiopharmaceuticals at its Radionuclide and Cyclotron Operations facility with the aid of model CS-30 Cyclotron. These radiopharmaceuticals are produced according to international standards of good manufacturing practice. The Research Centre meets the high standards of quality assurance and environmental safety with regard to radiopharmaceuticals.

Radiopharmaceuticals currently produced and available for distribution throughout the Kingdom and to adjoining Arab states are as follows: thallous (T1-201) chloride injection ($T^{1/2}$ = 73 h); gallium (Ga-67) citrate injection ($T^{1/2}$ = 78.3 h); iodine-123 capsules ($T^{1/2}$ = 13.1 h); iodine-123 oral solution ($T^{1/2}$ = 13.1 h); iodine-123 orthoiodohippurate solution ($T^{1/2}$ = 13.1 h); rubidium (Rb-81) → krypton (Kr-81 m) generator ($T^{1/2}$ = 4.58 h – 13 s); indium (In-111) oxine ($T^{1/2}$ = 67.92 h) for cell labeling; indium (In-111) DTPA for cisternography ($T^{1/2}$ = 67.92 h).

Suggestions from the medical community for additional cyclotron-produced needs are welcome.

Inquiries concerning the availability, price schedule, and technical information on specific radiopharmaceuticals should be directed to: Abbass H. Al-Marzouky, MD, Executive Director, Research Centre, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia (Fax No. 966-1-441-4839).

The Sandoz Prize for Immunology

Sandoz, the Swiss-based multinational pharmaceutical corporation, announces its biennial award, THE SANDOZ PRIZE FOR IMMUNOLOGY. The purpose of this award is to stimulate research projects leading to major improvements in health care. The prize will be awarded for the first time at the Congress of the American Association of Immunology in Washington in April 1990.

Of the $100,000 that make up the award, $80,000 will go to fund the awardee's project and the remaining $20,000 constitutes a personal recognition to the prize winner.

Sandoz has produced two of the major contributions to immunology in the past decade—Sandimmun and Sandoglobulin. Sandimmun is a selective immunosuppressant that made transplantation a viable therapeutic option. In addition, it is effective in the treatment of autoimmune diseases such as posterior uveitis, psoriasis, and nephrotic syndrome. Sandoglobulin was the first intact, fully functional human gammaglobulin that could be administered intravenously.

For further information concerning the prize, please contact: Sandoz Scientific Office, P.O. Box 7090, Jeddah 21462, Kingdom of Saudi Arabia.

King Faisal Specialist Hospital and Research Centre Symposia for 1410

King Faisal Specialist Hospital and Research Centre has scheduled the following postgraduate education symposia:

1. Symposium on Malignancies in Childhood, 6-7 February 1990 (11-12 Rajab 1410).
2. Third Annual Symposium on Excellence in Nursing, 26-28 February 1990 (1-3 Shaban 1410).
3. Symposium on Nonsurgical Management of Low Back Pain, 10-11 March 1990 (13-14 Shaban 1410).

For additional information, please contact the Director, Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia; telephone (01) 464-7272, extension 1837.

New Trends in Aortic Valve Surgery

A workshop on the topic "New Trends in Aortic Valve Surgery" is planned for 17-18 January 1990 at the King Faisal Specialist Hospital and Research Centre in Riyadh, Saudi Arabia. For information concerning the workshop, address correspondence to: Department of Cardiovascular Diseases, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia. FAX: (966-1) 441-4839.

Joint Board for Postgraduate Medical Education Symposia

The Joint Board for Postgraduate Education is pleased to announce the following symposia for 1410-1411 (1989-1990):

1. Geriatrics and Rehabilitation (location and dates to be announced).
2. 7th Annual Neurosciences, Riyadh Armed Forces Hospital, 10-11 Rajab 1410 (5-6 February 1990).
3. 5th Annual Paediatric Symposium, Security Forces Hospital, 7-8 Shaban 1410 (4-5 March 1990).
4. Recent Advances in Infectious Diseases, King Fahad National Guard Hospital, Riyadh, 25-26 Shawwal 1410 (20-21 May 1990).
5. Advances in Obstetrics & Gynaecology, Riyadh Armed Forces Hospital, 4-5 Rabi Al-Awal 1411 (23-24 September 1990).
6. Advances in Diagnostic Radiology, King Faisal Specialist Hospital and Research Centre, 11-12 Rabi Al-Awal 1411 (30 September-1 October 1990).
7. Advances in Thrombosis, King Faisal Specialist Hospital and Research Centre, 15-16 Jumada Al-Awal 1411 (2-3 December 1990).
8. 8th Annual Neurosciences, Riyadh Central Hospital, 27-28 Jumada Al-Thani 1411 (13-14 January 1991).
9. 6th Annual Paediatric Symposium, College of Medicine and King Khalid University Hospital, 26-27 Rajab 1411 (10-11 February 1991).
10. Gastroenterology and Hepatology, Security Forces Hospital, 10-11 Shaban 1411 (24-25 February 1991).
11. Postgraduate and Continuing Medical Education, College of Medicine and King Khalid University Hospital, 21-22 Shawwal 1411 (5-6 May 1991).

For further information, contact the Joint Board Office, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia; telephone (01) 467-1556 or 1564; telefax 481-1853; telex 403748 DARAYAH SJ.

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THE EDITORS of the *Annals of Saudi Medicine* welcome contributions from our readers. The *Annals* will consider for publication manuscripts of interest to readers in Saudi Arabia, the Middle East, and around the world. All submissions are subject to review by the Editorial Board and by referees in appropriate specialties.

Submission of Manuscripts. Manuscripts are received with the understanding that they are not under simultaneous consideration by another publication. An abstract published prior to a full report is not regarded as a duplicate publication. The author's transmittal letter must accompany the manuscript and contain these statements: "The manuscript has been seen and approved by all authors involved and is neither being published nor being considered for publication elsewhere. The authors transfer copyright to the *Annals of Saudi Medicine*." Accepted manuscripts may not be published elsewhere without *Annals'* permission.

Manuscript Preparation. The format of the *Annals of Saudi Medicine* complies with "Uniform Requirements for Manuscripts Submitted to Biomedical Journals," published by the International Committee of Medical Journal Editors in Vancouver, British Columbia, in 1979 (the widely accepted "Vancouver style"), as described in the *Annals of Internal Medicine* (1982; 96 [pt 1]: 766-71). With the exception of blood pressure, all units of measurement and laboratory values must be expressed in SI units; conventional units may be included parenthetically. Authors are referred to *Annals of Internal Medicine* (1987;106[1]:114-29) for guidance in the use of SI units. Manuscripts, including tables, references, and figure legends, must be typewritten, double-spaced, on $8^1/_2 \times 11$ inch (21.5 × 28 cm) or size A4 paper, with margins of at least 1 inch (2.5 cm). Pages should be numbered consecutively, beginning with the title page and continuing through the last page of typewritten material. One original and two photocopies of the entire manuscript should be submitted, along with three sets of photographs.

Title Page. The title page must contain (1) title of the article, (2) correct names of each author plus highest academic degree for each, (3) each author's official academic and/or clinical title and affiliation, (4) name and address of the institution(s), (5) name and address of author to whom correspondence should be sent, if it differs from the first author, and (6) any disclaimers. For case reports, it is recommended that the number of authors be limited to four. Acknowledgment of support should be included in the Acknowledgment section at the end of the article.

Abstracts. All original articles must contain an abstract of not more than 200 words. The abstract should include statements of problem, method of study, results, and conclusions.

Manuscript Format. Most original articles have the following format: Introduction (the question the paper intends to answer); Materials and Methods (the study design and methods, definitions such as for diagnostic criteria, the population or patient samples, and laboratory and statistical methods); Results (the pertinent findings in a logical sequence with tables and figures as necessary); and Discussion (conclusions based on the findings, evidence from the literature that supports the conclusions, conflicting evidence, applicability of the conclusions, and implications for future research or clinical applications). Authors might consult recent issues of the *Annals* for examples of appropriate format.

References. List references, double-spaced, in consecutive numerical order (the order of citation in the manuscript, not alphabetically). Once a reference is cited, all subsequent citations should be to the original number. All references must be cited in the text or tables. Unpublished data and personal communications will not be accepted as references. References to journal articles should include in this order, (1) authors, (2) title, (3) journal name (as abbreviated in *Index Medicus)*, (4) year, (5) volume and issue number, and (6) inclusive page numbers. References to books should include (1) authors, (2) chapter title (if any), (3) editors names (if any), (4) title of book, (5) city of publication, (6) publisher, and (7) year. Volume and edition numbers and specific page numbers should be included when appropriate. The author is responsible for the accuracy and completeness of the references and for their correct textual citation. Refer to reference citations and listings in the text for proper format.

Illustrations. Three copies of all figures or photographs should be included with the submitted manuscript. Photographs must be high-contrast, glossy, black and white prints, unmounted and untrimmed, with preferred size between 4 × 5 inches and 5 × 7 inches (10 × 13 cm and 13 × 18 cm). Color transparencies or photos will be accepted at the discretion of the Editorial Board. Figure number, name of senior author, and an arrow indicating "top" should be typed on a gummed label and affixed to the back of each illustration. Slides must be marked for "front" as well as "top." All lettering, arrows, or other artwork must be done by an artist or draftsman. Graphs and charts must also be prepared professionally by an artist or draftsman. Written permission must accompany any photograph in which the subject can be identified or any illustration that has been previously published. All illustrations ("figures") must be numbered as cited in the text in consecutive numeric order.

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Submit manuscripts to the Publications Office, *Annals of Saudi Medicine*, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia; telephone: (01) 464-7272, extension 1817.

amoxycillin

Prescribing Information

AMOXIL is a broad spectrum antibiotic suitable for a wide range of infections caused by susceptible organisms.

Indications
Respiratory, ear, nose and throat, genito-urinary and skin and soft tissue infections.

Dosage
Children: Oral and injectable – up to 2 years: 62.5mg–125mg every 8 hours. 2–10 years: 125mg–250mg every 8 hours. Based on bodyweight (including neonates) 35–100mg/kg/day.
Adults: Oral – 250–500mg every 8 hours. Injectable – I.M. 250–500mg every 8 hours or more frequently if necessary. I.V. 500mg–2g every 4–6 hours. (Doses in excess of 1g should be given by infusion over 30 minutes.)

Presentations
Capsules: maroon and gold capsules, each containing 250mg or 500mg amoxycillin*.
Syrup: 125mg amoxycillin* per 5ml.
Syrup Forte: 250mg amoxycillin* per 5ml.
Paediatric drops: 125mg amoxycillin* per 1.25ml in bottles with calibrated dropper.
Injection: Vials containing 250mg or 500mg amoxycillin as the sodiu salt.
*as the trihydrate.

Precautions
Reduced dosage is required in patients with impaired renal function.

Contra-indications
Penicillin hypersensitivity.

Side-effects
Side-effects, as with other penicillins, are usually of a mild and transitory nature; they may include diarrhoea, indigestion or an occasional rash, which may be either urticarial or erythematous: in either case it is advisable to discontinue treatment.

Further information is available from

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International Division 01/2131/6/88

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IMPORTANT NOTICE The World Health Organisation (WHO*) has recommended that pregnant women and new mothers be informed of the benefits and superiority of breastfeeding – in particular the fact that it provides the best nutrition and protection from illness for babies.
Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle-feeding or other foods and drinks should be discouraged since it will have a negative effect on breastfeeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breast-feed.
Before advising a mother to use an infant formula, she should be advised of the social and financial implications of her decision: for example, if a baby is exclusively bottle-fed, more than one can (450 g) per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breast-milk is not only the best, but also the most economical food for babies.
If a decision to use an infant formula is taken, it is important to give instruction on correct preparation methods, emphasizing that unboiled water, unboiled bottles or incorrect dilution can all lead to illness.

* See: International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34 22, May 1981

Information for the medical profession only.

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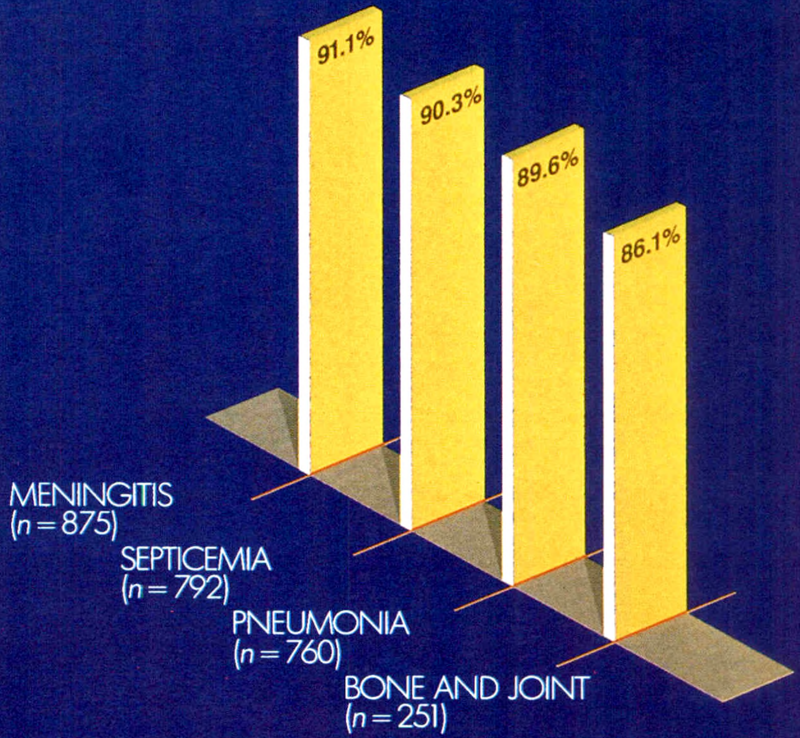

Components: Ceftriaxone. ***Indications:*** Sepsis; meningitis; abdominal infections; infections of the bones, joints, soft tissue, skin and of wounds; infections in patients with impaired defence mechanisms; renal and urinary tract infections; respiratory tract infections, particularly pneumonia, and ear, nose and throat infections; genital infections, including gonorrhea. Perioperative prophylaxis of infections. ***Dosage:*** Usual dosage for adults: 1–2 g once daily (every 24 hours). Further informations on administration and special dosage recommendations are available on request. ***Contra-indications:*** Known hypersensitivity to cephalosporins. ***Precautions:*** Pregnancy (particularly in the first trimester) unless absolutely necessary. Hypersensitivity to penicillin (possibility of allergic cross-reactions). Anaphylactic shock. ***Side effects:*** Gastrointestinal complaints. Hematological changes. Skin reactions. ***Packs:*** Packs for i.m. injection, 5's. Packs for i.v. injection, 5's. Packs for i.v. infusion, 5's. Full details are available on request.

Reference: Data on file, F. Hoffmann-La Roche Ltd, Basel, Switzerland

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المدونات الطبية السعودية مجلة تنشر بموجب الأمر الملكي السامي رقم ٥/م/٢٤٢٢٣ بتاريخ ١٤ شوال عام ١٤٠٠هـ. وتصدر مرة كل شهرين، وهي مشروع مشترك بين كل من كلية الطب ومستشفى الملك خالد الجامعي ـ جامعة الملك سعود، صندوق بريد ٢٩٢٥ ـ الرياض ١١٤٦١، المملكة العربية السعودية، ومستشفى الملك فيصل التخصصي ومركز الأبحاث، صندوق بريد ٣٣٥٤ ـ الرياض ١١٢١١، المملكة العربية السعودية. يتم صف وطبع المجلة بمطابع جامعة الملك سعود. كل المراسلات والاستفسارات وطرق الحصول على المستلات ترسل إلى مكتب المطبوعات على العنوان التالي:

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مستشفى الملك فيصل التخصصي ومركز الأبحاث
ص. ب ٣٣٥٤
الرياض ١١٢١١ ـ المملكة العربية السعودية

مندوب الاعلانات
بي آر سي المتحدة
ابسوم ـ سري ـ المملكة المتحدة

الآراء التي ترد في المقالات المنشورة تعبر عن رأي أصحابها فقط ولا تعبر عن وجهة نظر مجلة المدونات الطبية السعودية. لا يسمح بإعادة طبع أي جزء من المجلة أو نسخه بأي شكل وبأي وسيلة سواء أكانت إليكترونية أو آلية، بما في ذلك التصوير والتسجيل أو الإدخال في أي نظام حفظ أو استعادة معلومات إليكتروني، بدون الحصول على موافقة مسبقة من إدارة المجلة.

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- 96% success in skin infections[2]

1. Proceedings of Int. Symp. Excerpta Medica 1984, 54-67.
2. Roy. Soc. Med. Int. Cong. and Symp. Series **80**, 173-180.

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Activity BACTROBAN is a topical anti-bacterial agent, active against those organisms responsible for the majority of skin infections, eg *Staphylococcus aureus*, including methicillin-resistant strains, other staphylococci and streptococci. It is also active at concentrations attainable on the skin against Gram-negative skin pathogens such as *Escherichia coli* and Proteus spp.
Indications Bacterial skin infections, eg impetigo, folliculitis and furunculosis.
Dosage and Administration Adults and children: BACTROBAN should be applied to the affected area up to three times daily, for up to 10 days.
Precautions Avoid contact of BACTROBAN ointment with the eyes. Use BACTROBAN with caution in patients with moderate or severe renal impairment.
Use in Pregnancy There is inadequate evidence of safety to recommend the use of BACTROBAN during pregnancy.
Contra-indications Hypersensitivity to BACTROBAN or other ointments containing polyethylene glycols. This BACTROBAN formulation is not suitable for ophthalmic or intra-nasal use.
Side-effects Some minor localised effects such as burning, stinging and itching have been reported.
Storage BACTROBAN should be stored at room temperature (below 25°C).
Further information is available on request. BACTROBAN is a trademark.

International Division 001/34/2/7/89

Beecham Pharmaceuticals
BRENTFORD · ENGLAND

ANNALS OF SAUDI MEDICINE

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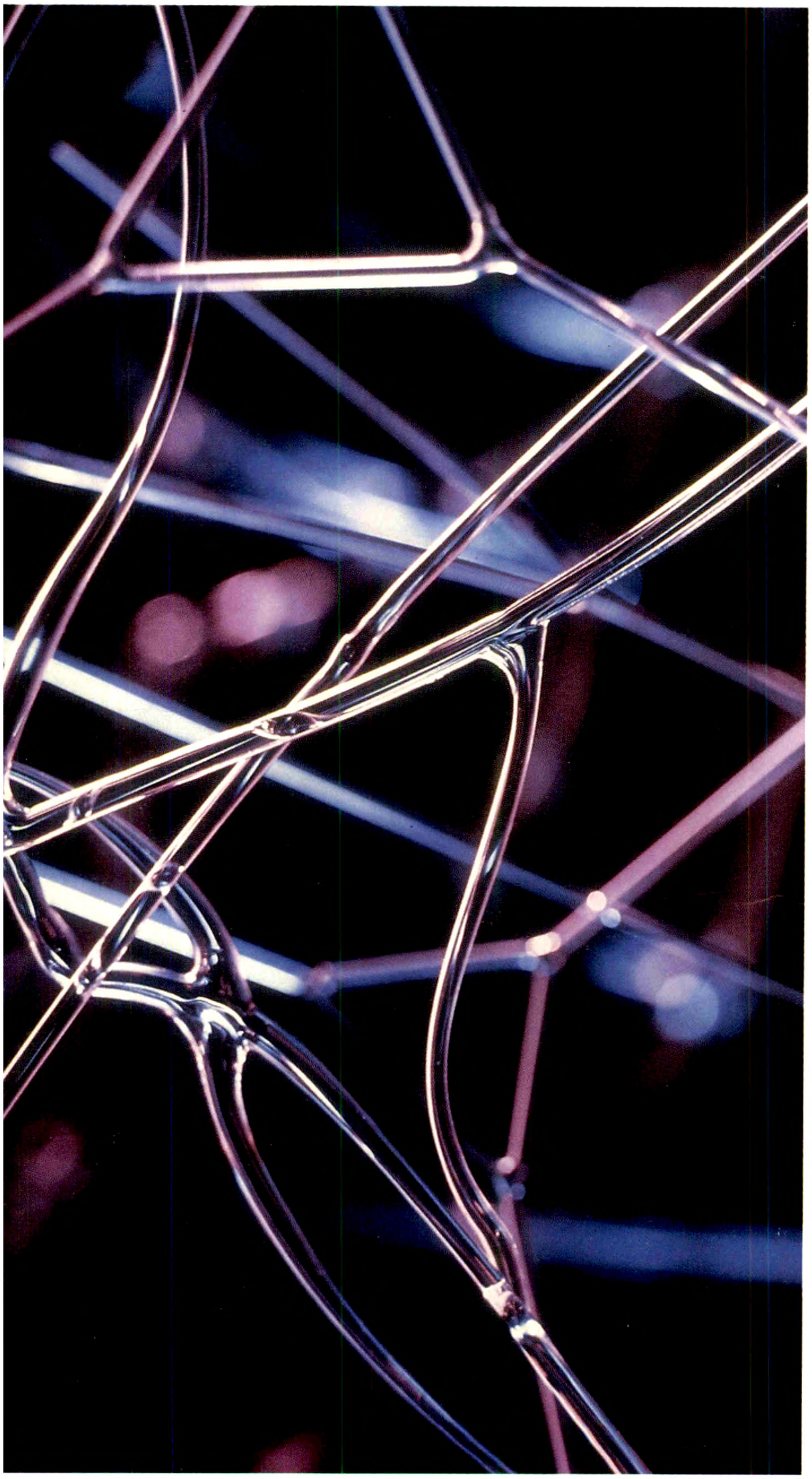
A BREAKTHROUGH IN CORONARY THROMBOLYSIS



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plasminogen
activator

The development of IV administered pharmacological agents to dissolve thrombi in coronary arteries represents a major therapeutic advance in the management of acute MI. Now, clinicians can actively intervene to interrupt the course of acute MI, establish reperfusion of ischaemic myocardium and thereby reduce mortality.

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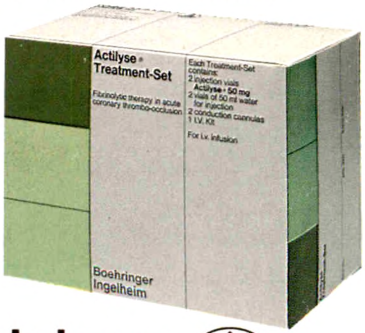
1. Van de Werf et al J Am Coll Cardiol 1988:12:14A-9A
2. TIMI Study Group N Engl J Med 1985:312 (14)932



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ANNALS OF SAUDI MEDICINE

Aims and Scope

The *Annals of Saudi Medicine* is a joint project of the King Faisal Specialist Hospital and Research Centre and the King Saud University College of Medicine and King Khalid University Hospital. The journal is typeset and printed at the King Saud University Press, Riyadh, Saudi Arabia. Since July 1985, the *Annals* has incorporated *The King Faisal Specialist Hospital Medical Journal*, established in 1980.

The *Annals* is a bimonthly multidisciplinary medical journal. High-quality papers, written in English, dealing with aspects of clinical, academic or investigative medicine or research will be welcome. Emphasis is placed on matters relating to medicine in Saudi Arabia in particular, and the Middle East in general, though articles are welcome from anywhere in the world, and the *Annals* has worldwide readership.

The *Annals* publishes original articles, case reports, letters to the editor, editorials, and from time to time, special communications, commentaries, and review articles. Abstracts of meetings and symposia sponsored by the Joint Board for Postgraduate Medical Education of Saudi Arabia are published, and the proceedings of such symposia may be published if the Editorial Board considers them appropriate and relevant. The Editorial Board wishes to minimize delay between manuscript submission, decision, and publication, and accordingly authors are requested to follow carefully the instructions set out under "Information for Authors."

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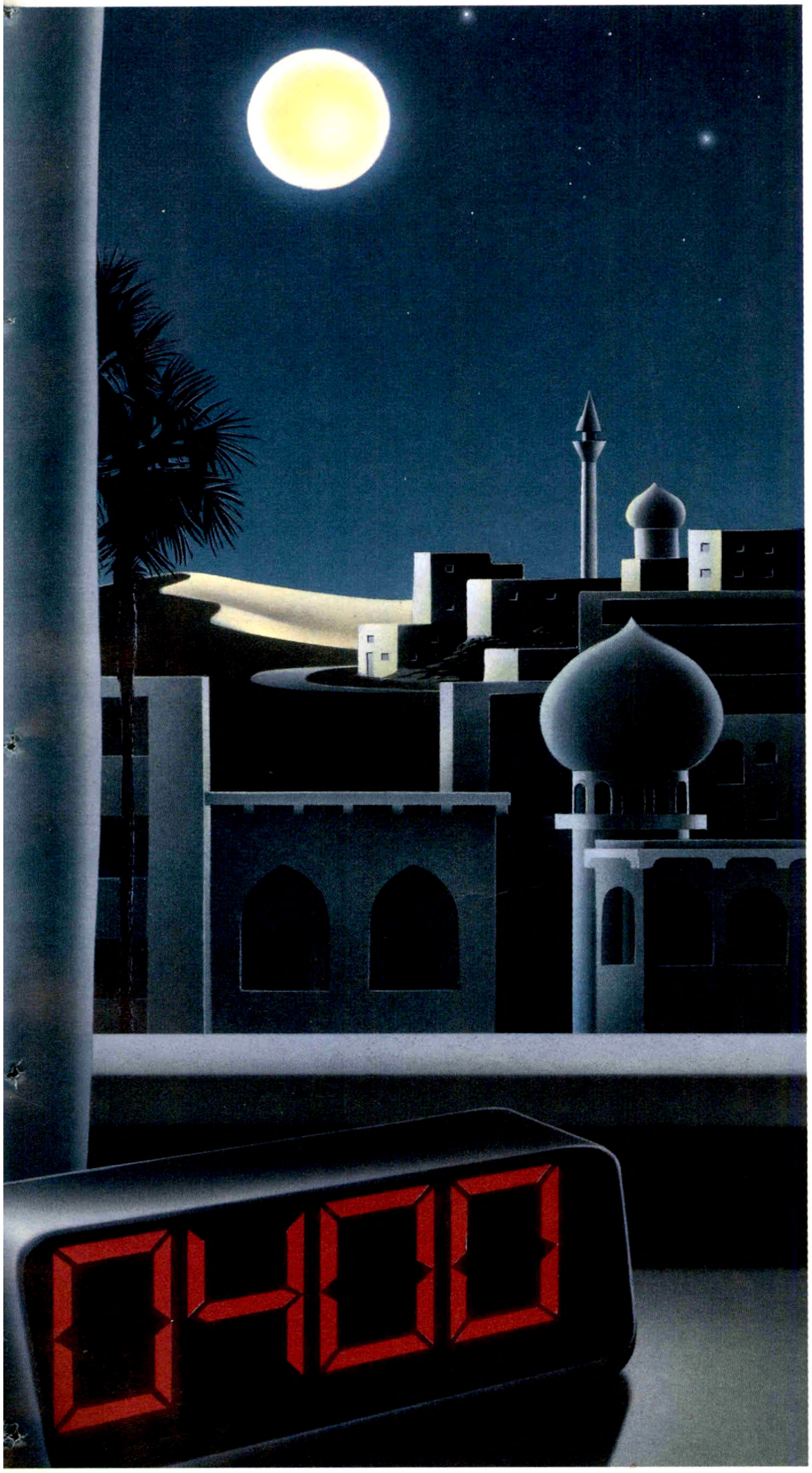

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1. Hanley SP, Nunn AJ: Clin. Trials J, Vol. 16, No. 2, 1979. pp. 34-36.
2. McIntosh D: Practitioner 227, November 1983. pp. 1757-1764
3. Riedel-Dibbern E, Leblanc K: J Clin Pharmacol, Suppl. 4. 1972, pp. 129-133.

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REFERENCES: 1. Roth SH, *Am J Med* 1987; **83** (Suppl 4B): 25–30. 2. Appelrouth DJ *et al*, *Am J Med* 1987; **83** (Suppl 4B): 78–81. 3. Carle WK, Rotman H, *R Soc Med Int Congr Symp Ser* 1985; (69): 139–148. 4. Brobyn RD, *Am J Med* 1987; **83** (Suppl 4B): 50–54.

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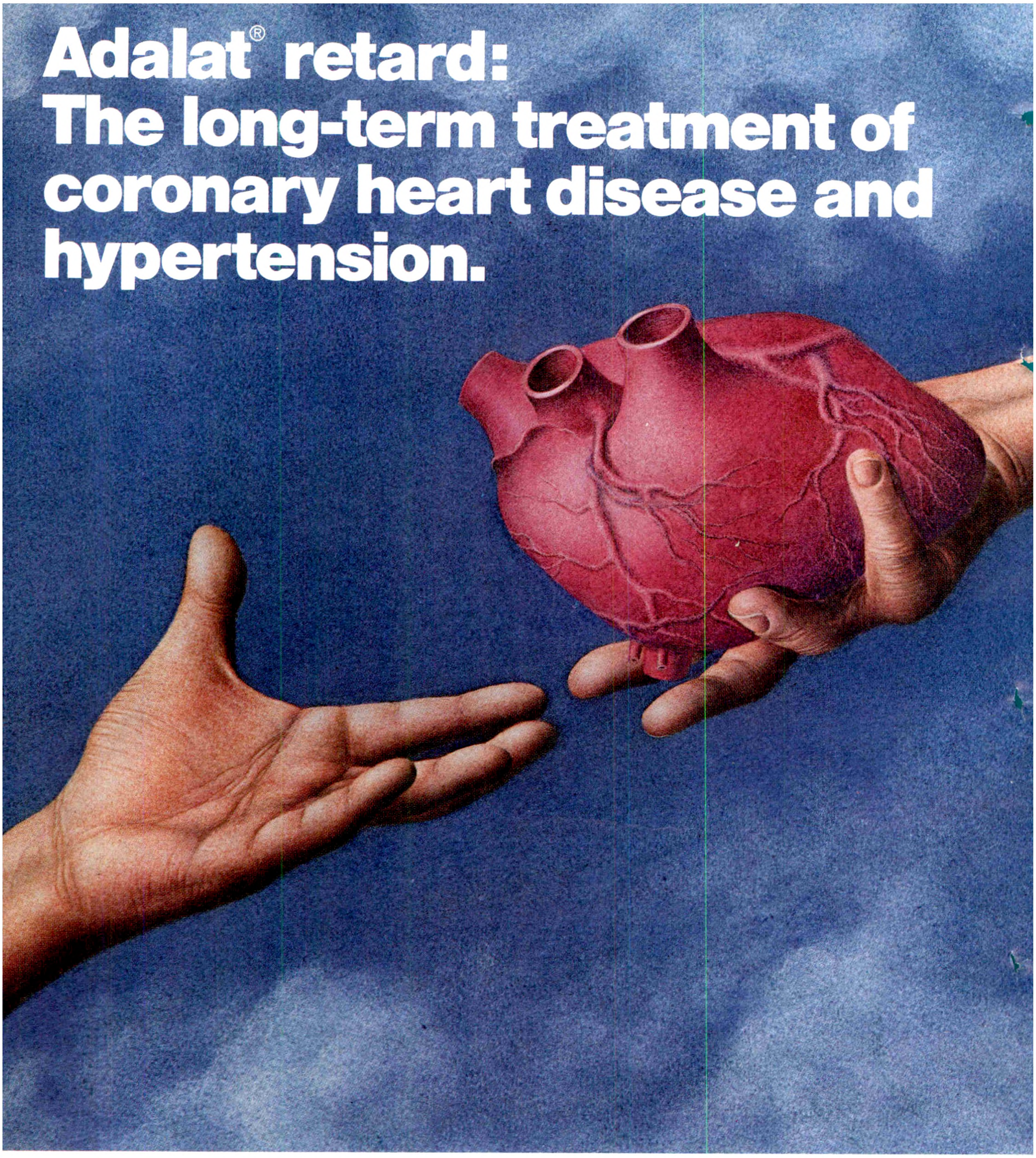
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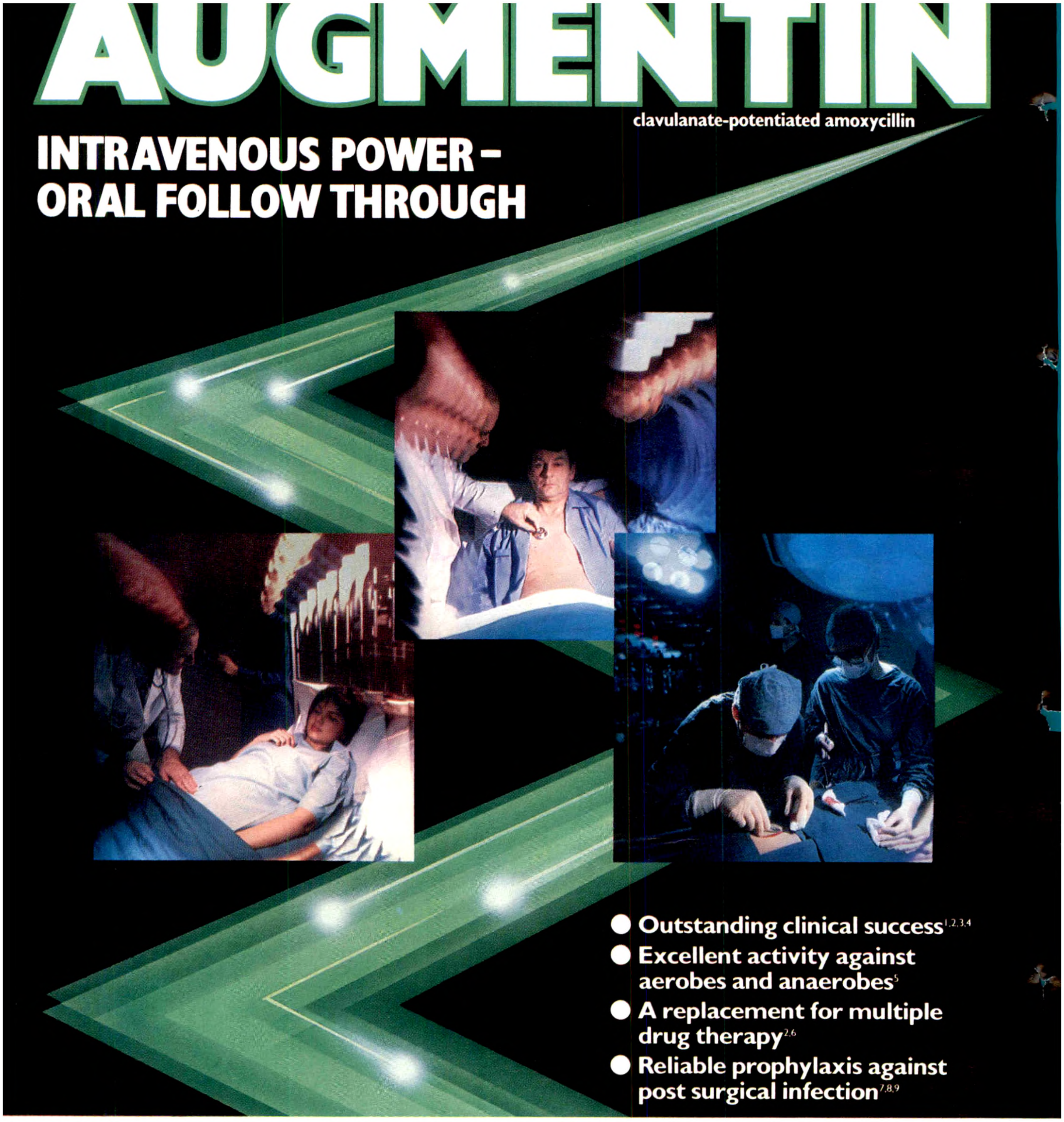
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Confidence

WHEN IMPAIRED HOST DEFENCES PUT PATIENTS AT RISK

Most hospitalised patients are to some degree immunocompromised and are therefore at special risk of infection.

Minor

- old age
- poor nutrition
- neonate
- catheters

Moderate

- surgery
- chronic debilitating diseases
- intensive care

Severe

- malignant disease
- prolonged neutropenia
- burns with loss of plasma

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Editorial

DILATED CARDIOMYOPATHY

Cardiomyopathies are classified into three groups: hypertrophic, restrictive, and dilated.[1] Dilated cardiomyopathy is defined as heart muscle disease of unknown cause represented by dilatation of the left or right ventricle or both.[1] Dilatation of the heart caused by alcohol intake or toxic, metabolic, or infectious agents should be excluded before diagnosing dilated cardiomyopathy.[2] The initial manifestation is cardiac enlargement and this can be revealed by routine chest roentgenogram and confirmed by echocardiography. At this stage the patient may be totally asymptomatic. Later on the patient may exhibit symptoms of left ventricular failure, arrhythmia, or chest pain; congestive cardiac failure may occur as a late manifestation.

The right ventricle is preferentially involved in some cases of dilated cardiomyopathy. This type of right ventricular cardiomyopathy (also known as right ventricular dysplasia, arrhythmogenic right ventricular dysplasia, Uhl's anomaly, and parchment heart) may be familial or acquired.[3-5]

The incidence of dilated cardiomyopathy is largely unknown. In a study from King Khalid University Hospital, Riyadh, 101 cases were identified over four years.[6] The Mayo Clinic reported 104 cases during 14 years of follow-up.[7]

In this issue of the *Annals*, Nouh and Qaraqish report on the occurrence of arrhythmia in dilated cardiomyopathy. In their study, Holter monitoring was used to evaluate 60 consecutive patients with dilated cardiomyopathy. Forty percent of their cases had supraventricular tachycardia while 30% had ventricular tachycardia. During follow-up, four of their patients sustained recurrent episodes of ventricular tachycardia and died.

Some workers have found that complex ventricular ectopy shown by Holter monitoring is an independent predictor of mortality,[8-10] though others found no correlation.[11,12] While there is no evidence that antiarrhythmic drugs prolong life or prevent sudden cardiac death in cases of dilated cardiomyopathy, they are appropriate in the treatment of symptomatic or serious arrhythmias.[13] However, most antiarrhythmic agents depress myocardial contractility and may do more harm than good when ventricular function is impaired.

In view of the high incidence of thromboembolic complications, all patients with dilated cardiomyopathy and chronic heart failure should receive anticoagulant therapy,[14] unless there is a contraindication.[14] Approximately 15% of the patients who recover from clinically diagnosed acute viral myocarditis have residual chronic cardiac disease in the form of dilated cardiomyopathy.[15] Active myocarditis is identified from biopsy specimens in some cases of dilated cardiomyopathy. The use of immunosuppressive therapy in dilated cardiomyopathy is still controversial.

A heterogeneous group of patients with dilated cardiomyopathy was studied by Parrillo et al.[16] Patients were assigned randomly to receive prednisone or placebo, and randomization was stratified according to the presence or absence of indicators of myocardial inflammation. Initially 60 mg of prednisone was given daily for three months then on alternate days for six months. At three months, improvement, defined prospectively as an increase in ejection fraction of ≥5 percentage points, was observed in 53% of the patients receiving prednisone and 27% of controls. This small increase was not observed at nine months. The authors concluded that prednisone has only marginal clinical benefits and should not be administered as standard therapy in cases of dilated cardiomyopathy.

The natural history of the disease varies. Death may ensue within two years in 50% of afflicted patients[7] while survival for more than 10 years has been observed in 25% of the cases. Significant cardiomegaly, low cardiac output, and frank congestive heart failure are associated with poor prognosis.[17,18] Cardiac transplantation has proved to prolong the life of patients with dilated cardiomyopathy and should be considered before secondary changes in systemic pulmonary circulation become irreversible.

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Original Articles

ACUTE MYOCARDIAL INFARCTION IN THE EASTERN PROVINCE OF SAUDI ARABIA: RETROSPECTIVE ANALYSIS OF 264 PATIENTS

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أجريت دراسة مراجعة على ٢٦٤ ملف لمرضى أدخلوا إلى مستشفى الملك فهد في الفترة ما بين يناير ١٩٨٢م وديسمبر ١٩٨٧م، وشخصت حالاتهم على أنها احتشاء حاد مؤكد في عضلة القلب. كان إجمالي عدد الذكور ٢٢١ (نسبة ٨٤٪) وعدد الإناث ٤٣ (نسبة ١٦٪) وكان متوسط العمر ٥٣,٢ ± ١٢,٣ عامًا. شكل السعوديون نسبة ٦١٪ من المرضى وكان الهنود والباكستانيون من الجنسيات الأكثر تواردًا بين غير السعوديين (نسبة ١٦٪). كانت أكثر عوامل التعرض التي صادفناها التدخين (نسبة ٥٧٪) وتاريخ مرضي للإصابة بداء القلب الإكليلي (نسبة ٤٨٪)، وداءالسكري (نسبة ٢٨٪). توفي في المستشفى ٥٤ فردًا من مجموع المرضى (نسبة ٢٠٪) بسبب مضاعفات ذات علاقة بالإحتشاء الحاد في عضلة القلب. حدّد التحليل الراجع أن الصدمة القلبية، وتوقف القلب، وحدوث قصور القلب الاحتقاني الشديد ثلاثة عوامل سيئة أثرت منفردة على وفيات المرضى في المستشفى. كما جرى تحليل حالة ٢٠٨ مرضى جرت متابعتهم لفترة متوسطها ٣٢ شهرًا فيما يتعلق بعوامل البقيا على المدى الطويل. وبالرجوع إلى منحنى البقيا قدر احتمال البقيا لفترة ٣٦ شهرًا على أنه ٠,٧٨ ± ٠,.٦ (٩٥٪ درجة الوثوق، ٦٦ إلى ٩٠٪). أظهر تحليل الخطر النسبي مع وجود متغيرات عديدة (طريقة كوكس) أن تجاوز سن الستين، وقصور القلب الاحتقاني الشديد والتوقف عن استخدام النترات مديدة التأثير كانت لوحدها هي المتغيرات المهمة التي أثرت سلبيًا وبشكل مستقل على البقيا لفترة طويلة. تشير معطياتنا إلى ضرورة زيادة الجهود في مكافحة التدخين. علاوة على ذلك ينبغي مقارنة المعلومات الأساسية التي حصلنا عليها من هذا التحليل مع ما يستقى من وحدة الرعاية الإكليلية التي أسّست حديثا. تشير البيانات أيضا إلى أهمية تقييم الدور الوقائي للنترات مديدة التأثير.

The medical records of all patients (N = 264) admitted to King Fahd Hospital with a confirmed diagnosis of acute myocardial infarction (AMI) between January 1982 and December 1987 were retrospectively reviewed. A total of 221 males (84%) and 43 females (16%) were identified. Median age was 53.2 ± 12.3 years. Saudi patients constituted 61% of the patients, and Indians and Pakistanis were the most frequent nationalities among non-Saudis (16%). Current smoking history (57%), past medical history of coronary heart disease (48%), and diabetes mellitus (28%) were the most common risk factors encountered. Of all the patients, 54 (20%) died in hospital from AMI-related complications. Logistic regression analysis identified cardiogenic shock, cardiac arrest, and development of severe congestive heart failure (CHF) as three adverse factors that, independently, influenced in-hospital mortality. Over a median follow-up of 32 months, 208 patients were analyzed for long-term survival. The survival curve estimated that at 36 months the survival probability (±SE) was 0.78 ± 0.06 (95% confidence interval, 66 to 90%). The multivariate proportional hazard of Cox revealed that age above 60 years, severe CHF, and withholding long-acting nitrates were the only significant covariates that independently influenced long-term survival adversely. Our data indi-

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cate that efforts to combat smoking should be intensified. Furthermore, the baseline information obtained from our analysis should be compared with that derived from our newly established coronary care unit. The data also indicate that the prospective evaluation of the protective role of long-acting nitrates is warranted.

Despite the recently reported decline in the mortality rates of coronary heart disease (CHD)[1,2] and the improved survival after acute myocardial infarction (AMI),[3,4] AMI remains a major cause of adult mortality in Western societies. In Western populations, World Health Organization statistics indicate that CHD accounts for more than one-third of all male deaths between the age of 45 and 54 years.[5] In the United Kingdom, approximately 160,000 deaths occur each year as a result of CHD.[6] Conversely, lower mortality rates from CHD have been noted in developing communities. However, immigration studies have shown that the incidence of CHD and its resultant mortality can rise with urbanization and modernization of life-style.[7,8] Recent data have shown that lower-risk individuals of Asian origin exhibit an increased susceptibility and suffer worse CHD than do Asians remaining in their own countries and the indigenous population of the country of adoption.[9,10]

In the past twenty years, Saudi Arabia has witnessed gigantic socioeconomic progress, with social and dietary habits and life-style that now resemble those of Western countries. These changes have been accompanied by an appreciable increase in the number of patients with CHD seen at major hospitals. However, insufficient epidemiological data exist concerning the actual prevalence of the disease and its known risk factors. Thorough search of the Saudi Medical Bibliography between 1887 and 1984 failed to identify any published article relating to the disease.[11] Furthermore, Medline literature search back to 1966, using *Arabia* and *myocardial infarction* or *angina pectoris* as medical subject headings, did not reveal any pertinent publication.

The importance of obtaining baseline data on CHD and AMI in Saudi Arabia, the prevalence of risk factors among AMI patients, and the prognostic variables that determine survival prompted this retrospective analysis. Another objective was to provide local data for future assessment of the impact of a coronary care unit on mortality. Only by comparing mortality data on AMI patients managed in an intensive care unit with that obtained in patients treated in our newly established coronary care unit can meaningful conclusions concerning the benefits of the latter be drawn.

Material and Methods

The medical records of all patients admitted to King Fahd Hospital of the University with a confirmed diagnosis of AMI between January 1982 and December 1988 were retrospectively reviewed. A confirmed diagnosis of AMI was based on World Health Organization diagnostic criteria.

Data Analysis and Statistical Methodology

A computerized database was constructed to include patient identification and all relevant clinical, laboratory, electrocardiographic, echocardiographic, and radiological data. Because of the retrospective nature of the study, patients were considered to have congestive heart failure (CHF) only if their medical records clearly indicated class III or IV CHF according to New York Heart Association criteria. Also included in the database were therapy details, course and complications, and follow-up information (Table 1). Continuous variables were used, both as continuous or categorized covariates, using different cutoff points. The models, however, included either continuous or categorized variables, whichever produced statistical significance.

Exploratory univariate data analysis was first carried out to determine the unadjusted influence of variables on the probability of in-hospital mortality. Chi-square and Fisher's exact test were used to estimate such unadjusted effects.[12] Variables found significant at the 0.05 level were included in a stepwise logistic regression model to determine their adjusted influence.[13] Covariate interactions were not explored in the regression model. Two goodness-of-fit tests were employed to ascertain that the logistic model is appropriate,[14] and the predicted values fit the data.[15]

TABLE 1. *Retrieved retrospective data for patients with acute myocardial infarction.*

Patient Characteristics
- Age
- Sex
- Nationality
- Adiposity Index
- Occupation
- Marital status

Risk Factors
- Smoking
- Diabetes
- Hypertension
- Hyperlipidemia
- Ischemic heart disease
  - Nature
  - Duration
  - Therapy
  - Control
  - Complications
- Family history

Clinical Data
- Duration of chest pain
- Associated symptoms
- Blood pressure
- Pulse
- Jugular venous pressure
- Cardiomegaly
- Pulmonary congestion

Investigations
- Electrocardiographic data
- Chest roentgenogram
- Lipids
- Fasting and random blood sugar
- Cardiac enzymes*
- Others

Complications
- Arrhythmias
- Conduction defects
- Hypotension
- Cardiogenic shock
- Cardiac arrest
- Immediate post-AMI angina
- Reinfarction
- Congestive heart failure

Therapy
- Nitrates
- Digoxin
- Beta blockers
- Calcium channel blockers
- Other antiarrhythmics
- Antiplatelets
- Diuretics
- Others

Follow-up events
- Death
- Heart failure
- Reinfarction
- Angina
- Others

Follow-up therapy
- All therapy details and compliance

*Cardiac enzymes were included in the analysis at their baseline and highest values, and the interaction of the highest values and the day of documentation.
AMI = acute myocardial infarction

Long-term survival was only estimated for those patients who survived the AMI and were discharged alive from the hospital. This latter "conditional survival" analysis was performed to avoid the possible bias introduced by comparing the survival of those who died early and those discharged alive.[16] The exclusion of early deaths from the analysis of long-term survival should eliminate those factors that primarily influence in-hospital mortality and determine those covariates that influence survival following hospitalization. Survival duration was estimated from the date of documentation of AMI until the date of death or last contact. Unadjusted plots that estimated cumulative and median survival were produced by the Kaplan-Meier method.[17] The log-rank test was used to assess the significance of unadjusted differences in survival for each prognostic factor.[18] Variables significant at the 0.05 level were included in a multivariate regression analysis using the proportional hazards model of Cox.[19] No interactions between variables were explored. The hazard rate $[h(t;x)]$ for the model can be written as: $h(t/x) = h\mathit{o}\,(t)\exp(\mathit{B}x)$ where t denotes time to event, x is the covariate vector, and *B* is the corresponding vector coefficient estimated by fitting the model. The term $h\mathit{o}(t)$ represents the hazard when all covariates are at baseline values. Covariates were entered into the model using a forward stepwise selection procedure. The results from the proportional model were used to divide patients into two patterns (low and high risk groups) according to their estimated hazard.

In all data analysis, $P < 0.05$ was considered significant. The statistical analysis was performed using the P4F, PLR, PIL, and P2L programs of the BMDP statistical software package.[20]

Results

From January 1982 to December 1988, 264 patients were admitted with a confirmed diagnosis of AMI. There were 221 (84%) males and 43 (16%) females, with a median age ± SD of 53.2 ± 12.3 years. Thirty patients (11%) were below age 40, 160 (61%) were between 41 and 60, and 74 (28%) were older than 60 years. Of the 264 patients, 170 (64%) were Saudis. Indians and Pakistanis together constituted about 16% of all patients. The mean age of the Saudi patients was not significantly different from that of Indians and Pakistanis. There was no other dominant nationality in our studied population. Table 2 shows the distribution of CHD risk factors in the studied population. Current smoking history (57%), past medical history of ischemic heart disease (48%), and diabetes mellitus (28%) were the most common risk factors.

TABLE 2. *Distribution of coronary heart disease risk factors.*

Risk factor	No. of patients
Smoking	151(57%)
Prior CHD history	
Angina	108(41%)
AMI	8(3%)
Angina and AMI	11(4%)
Diabetes mellitus	74(28%)
Hypertension	71(27%)
Abnormal fasting	
Cholesterol	56(21%)
Triglyceride	49(19%)
CHD family history	21(8%)

CHD = coronary heart disease; AMI = acute myocardial infarction.

MB creatine kinase fraction and echocardiographic data were only available for 5% and 8% of patients, respectively. Therefore, these two variables were not analyzed. Furthermore, none of our patients underwent intraaortic balloon counterpulsation or coronary angioplasty, and therefore these therapeutic interventions were not included. As only three patients underwent coronary bypass surgery, this procedure was also not used as a covariate in the assessment of long-term survival.

During the first hospitalization, 54 patients (20%) died as a result of AMI-related complications. Univariate unadjusted analysis identified several significant variables that adversely influenced in-hospital mortality (Table 3). However, adjustment of these factors using the stepwise logistic regression model identified only three independent risk factors: cardiogenic shock (91%), cardiac arrest (95%), and severe CHF (72%) (Table 4). The goodness-of-fit tests of Brown[14] and Hosmer[5] confirmed that the logistic model is appropriate and the predicted values fit the data. According to the logistic regression equation, the presence of all three adverse prognostic factors predicts an in-hospital mortality of >0.99. Conversely, in the absence of these three factors, the probability of hospital death is <0.006.

TABLE 3. *The unadjusted influence of covariates on the probability of in-hospital mortality.*

Variable	Unfavorable (%)	Favorable	*P* value
Age	Above 60 years (28)	Below 60 years	0.0205
Sex	Females (16)	Males	0.0081
Dyspnea	Present (35)	Absent	0.0296
Orthopnea	Present (9)	Absent	0.0254
Blood pressure (mm/Hg)			
Systolic	< 100 (18)	> 100	0.0004
Diastolic	< 60 (10)	> 60	0.0006
Cardiac shock	Occurred (12)	Absent	< 0.0001
Severe CHF	Occurred (11)	Absent	< 0.0001
Sinus tachycardia	Occurred (20)	Absent	< 0.0001
PVC	Occurred (17)	Absent	< 0.0001
VFA	Occurred (5.5)	Absent	< 0.0001
Cardiac arrest	Occurred (8)	Absent	< 0.0001
AV block	Occurred (12)	Absent	< 0.0001
Blood glucose			
Fasting	> 140 mg/dL (31)	< 140 mg/dL	0.0058
Random	> 250 mg/dL (21)	< 250 mg/dL	< 0.0001
CPK	> 3,000 IU/dL (8.7)	< 500 IU/dL	0.0063
LDH	> 2,000 IU/dL (11.5)	< 300 IU/dL	< 0.0001
Beta blockers	Not given (74)	Given	< 0.0001
Calcium channel blockers	Not given (65)	Given	< 0.0024
Long-acting nitrates	Not given (19)	Given	< 0.00001
Old MI	Present in ECG (9.5)	Not present	0.0018

CHF = congestive heart failure; PVC = premature ventricular contractions; VFA = ventricular fibrillation or asystole; AV = atrioventricular second or third degree block; CPK = maximum level of creatine kinase; LDH = maximum level of lactic dehydrogenase; MI = myocardial infarction; ECG = electrocardiogram.

Of the 210 patients who survived the AMI and were discharged alive, two were lost early to follow-up and excluded from further analysis. Over a median follow-up period of 32 months, a further 18 (8.7%) patients died due to the cardiovascular causes. The tail of the survival curve (Figure 1) is based on survival estimates from only two patients who were followed the longest (65.94 and 80 months) and who died. Ignoring the tail of the curve because of its known unreliability allowed certain survival estimates. At 36 months, the cumulative survival probability (± SE) was 0.78 ± 0.06 (95% confidence limit, 66 to 90%). The data of all 208 patients were examined to identify the effect of various prognostic factors on survival. Table 5 depicts the results of the univariate analysis. Several factors were found to influence the probability of death from cardiovascular-related causes. Inclusion of all the unadjusted factors with $P < 0.05$ into the multivariate regression analysis model of Cox identified only three risk factors that independently affected long-term survival: age above 60 years, withholding long-acting nitrates, and development of severe CHF (Table 6). Table 6 also shows that, while the occurrence of severe CHF was included in the model, its P value did not reach a significant level.

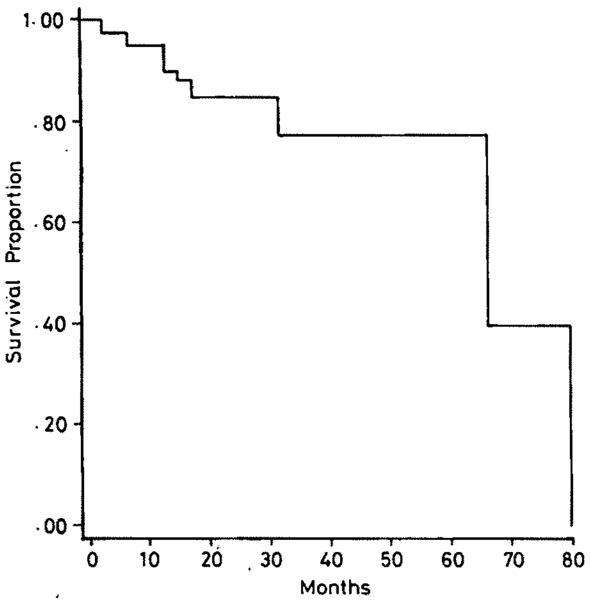

FIGURE 1. Survival curve of the 208 patients with acute myocardial infarction.

Based on the proportional hazards model, the survival curves of two prognostic patterns were predicted (Figure 2). The first survival pattern represents the group of patients possessing none of the unfavorable prognostic covariates of long-term survival; the second pattern represents the group with all three variables. While the 50-month median survival for the first group had not been reached at the time of this report, the median sur-

TABLE 4. *The adjusted influence of covariates on the probability of hospital death (stepwise logistic regression model).*

Variable	Coefficient	SE	Coefficient/SE	*P* value
Constant	−0.49266	1.062	−0.4637	–
Cardiogenic shock	−1.6421	0.3921	−4.187	< 0.0001
Cardiac arrest	−2.4750	0.6570	−3.767	< 0.0001
Severe CHF	−0.91283	0.2907	−3.140	< 0.0001

SE = standard error; CHF = congestive heart failure.

TABLE 5. *The significant covariates that adversely influenced long-term survival based on univariate analysis.*

Variable	Unfavorable (%)	Favorable	*P* value
Age	Above 60 years (24)	Below 60 yerars	0.0031
PVC	Occurred (12.5)	Absent	0.0062
Cardiogenic shock	Occurred (1)	Absent	0.007
Severe CHF	Occurred (5)	Absent	0.0254
Long-acting nitrate	Not given (20)	Given	0.0028

PVC = premature ventricular contractions; CHF = congestive heart failure.

TABLE 6. *Multivariate analysis of covariates predicting long-term survival.*

Variable	Unfavorable	Favorable	Coefficient	*P* value
Age	> 60 years	< 60 years	0.9986	0.013
Long-acting nitrates	Not given	Given	−1.8437	0.031
Severe CHF	Occurred	Absent	0.8433	0.067

*Using the proportional hazard model of Cox.
CHF = congestive heart failure.

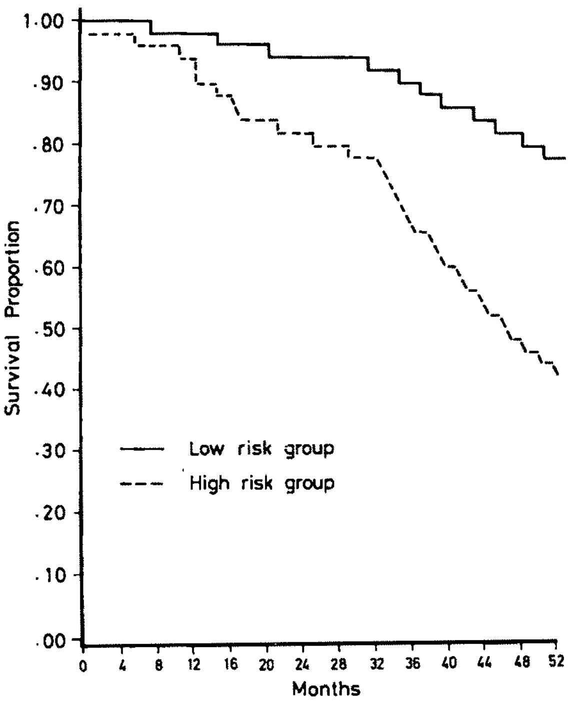

FIGURE 2. The survival curves of the two prognostic patterns for the low- and high-risk groups.

vival of the second group was about 42 months.

Discussion

The actual prevalence of CHD in Saudi Arabia is yet to be adequately determined. We retrospectively analyzed 264 patients with a confirmed diagnosis of AMI seen over a six-year period at a tertiary care facility to provide useful baseline information about the disease in the Kingdom, but the problems inherent in such a retrospective study should not be underestimated.

Males constituted about 84% of the study population. This degree of male preponderance is slightly higher than that reported from industrialized countries.[6,21] However, the higher proportion of male patients could be explained by the inclusion of expatriates who are predominantly male and constituted 36% of the study population. Indians and Pakistanis together were the second largest group, comprising about 16% of all patients. This latter proportion strengthens the existing belief about the increased prevalence of CHD among these two nationalities, which has been attributed to the presence of substantial amounts of cholesterol oxides in their diet.[22] However, contrary to the general impression, we found no significant difference between the mean age of Indians and Pakistanis and that of Saudis.

A history of current smoking was the most dominant risk factor—57% of all patients. This figure is comparable to that noted for AMI populations in New Zealand.[23] The high prevalence of smokers in our patient population indicates the need for a more effective antismoking campaign in Saudi Arabia. In the United States, about 24% of the estimated decline in the mortality from ischemic heart disease was attributed solely to a reduction in cigarette smoking.[1] History of previous CHD was the second most frequent risk factor and was present in 48% of our patients. In our study population, the prevalences of diabetes mellitus (28%) and hypertension (23%) were less than those reported in black Americans with AMI, but higher than those found in white Americans.[24]

The 20% in-hospital case-fatality rate in our series is comparable to the 23% reported in a 1970 survey of 33 acute care hospitals in the United States.[1] However, more recently, better results of about 10 to 17% have been reported.[4,25] The relatively increased mortality in our hospital could be attributed to several reasons. First, more than 95% of the studied population were admitted to a multidisciplinary intensive care facility and not to a coronary care unit, which has only recently become available. In several large studies, it was shown that coronary care units account for about 5 to 13.3% of the estimated decline in CHD mortality rates.[1,2] Second, our hospital is a tertiary care facility and thus frequently receives poor risk patients with various complications who have received inadequate care at the referring hospital, and such bias in the referral pattern influences the mortality data. Third, our intensive care unit was not designed or equipped to provide support for invasive cardiology. Fourth, because of a staffing shortage, cardiac patients were looked after mainly by general internists and not by cardiologists.

While several factors were found to influence in-hospital mortality before unadjusted analysis, adjusted logistic regression identified only three independent prognostic variables that adversely affected survival during the first hospitalization. These factors were cardiogenic shock, development of severe CHF, and cardiac arrest, occurring in 12%, 11%, and 8% of all patients, respectively. Furthermore, our data have shown that the presence or absence of these three factors together was associated with a 0.99 or 0.006 probability of in-hospital death, respectively. The adverse prognostic influence of cardiogenic shock and severe CHF seen in our series is in keeping with the well-known poor outcome from these two complications.[5] However, the in-hospital mortality rate from severe CHF in our series (72%) is relatively high. Conversely, in a recently published series,[4] the presence of rales and third heart sound at the onset of AMI was associated with mortality rates of up to 64% and 60%, respectively, over a four-year follow-up. However, data about in-hospital mortality from severe CHF complicating AMI were not reported. Regarding cardiac arrest, the nature of the retrospective analysis did not always allow clear distinction between cardiac arrest due to primary and secondary ventricular fibrillation. The poor prognostic outcome of patients who developed primary ventricular fibrillation following AMI was recently reported.[26] A twofold increase in the relative risk of dying was demonstrated in the patients with primary ventricular fibrillation compared to a well-matched reference group of patients derived from the same coronary care units. A similar observation was also reported from another European study.[27] Secondary ventricular fibrillation in the presence of severe but not uniformly fatal CHF could lead to a mortality rate as high as 70%.[1,28] The poor outcome of our patients with severe CHF and cardiac arrest in our series could also be explained by factors described earlier.

The MB fraction of creatine kinase provides an estimate of the AMI size and predicts early morbidity and mortality.[29] Unfortunately, the prognostic significance of this inexpensive, noninvasive, and readily available method could not be tested in our retrospective analysis.

Long-term survival analysis over a median follow-up of 32 months has shown that 78% of patients were alive at 36 months, (95% confidence interval, 66 to 90%). The survival data were similar to those reported elsewhere.[4] Unadjusted analysis identified several adverse prognostic factors, but adjustment using the multivariate regression proportional hazard of Cox identified only three factors. Patients older than 60 years showed a higher mortality than those who were younger. Similarly, old age was the only independent prognostic variable found to have an adverse effect on outcome in 1196 cases of AMI reported in a large study.[23] The negative influence of severe CHF on long-term survival is expected and is in direct proportion to the size of the infarct. Data regarding the assessment of myocardial function using echocardiographic estimation of left ventricular ejection fraction was only available for a small portion of the revised medical records. The prognostic significance of such a tool has been recently documented.[30] Our model has also shown that long-acting nitrates provide protection. It has been reported that the medical management of clinical ischemic heart disease accounted for an approximate 10% decline in CHD mortality.[1] However, this benefit has been mainly attributed to the use of beta-adrenergic blocking agents.[31] The protective effect of long-acting nitrates has not been proven, but it is conceivable that long-acting nitrates acting as vasodilator agents might be beneficial in those patients who sustain post-AMI heart failure.[32] Conversely, the retrospective nature of our study prevents adequate assessment of the usefulness of long-acting nitrates, particularly without data on patient compliance in taking administered medications. This needs to be tested prospectively.

A great deal of information about coronary heart disease in Saudi Arabia is yet to be obtained. Our retrospective analysis of 264 patients attempts to provide some baseline data about AMI in the Kingdom. The prevalence of known risk factors was analyzed, and history of current smoking was the most frequently encountered. This emphasizes the need for a more effective antismoking campaign. The analysis also revealed certain prognostic factors that influence in-hospital mortality and long-term survival, and our study should be replicated in other centers. In the future, our retrospective data will be compared with those derived from our newly established well-equipped coronary care unit.

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ARRHYTHMIAS IN DILATED CARDIOMYOPATHY: INCIDENCE, CLINICAL SIGNIFICANCE, AND PROGNOSTIC PATTERN

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تشكل اضطرابات النظم بفئاتها المتنوعة خطرًا على حياة المصابين باعتلال عضلة القلب التوسعي الغامض. وقد أجريت محاولة لدراسة هذه الاضطرابات بالمراقبة المديدة بمنظر هولتر. شملت الاضطرابات الناشئة فوق البطين مركبات أذينية مبتسرة في ٣٠٪، ورجفانًا أذينيًا مزمنًا في ٣, ٢٣٪، وتسرعًا فوق بطيني في ٤٠٪ من الحالات. تظاهر اختلال النظم البطيني بابتسار ضربات منتبذة بطينية متجانسة في ١٥٪، وضربات منتبذة بطينية متعددة الأشكال في ٦٠٪ وتسرع بطيني في ٣٠٪ من الحالات. عانى أربع من مرضانا من نوبات متكررة من التسرع البطيني. وتوصلنا إلى أنه كلما زادت خباثة اضطراب النظم ازداد خطر وفاة هؤلاء المرضى.

Arrhythmias of various categories may endanger the lives of patients with idiopathic dilated cardiomyopathy. An attempt was made to study these arrhythmias by long-term Holter monitoring. Arrhythmias of supraventricular origin included premature atrial complexes in 30%, chronic atrial fibrillation in 23.3%, and supraventricular tachycardia in 40% of the cases. Ventricular dysrhythmias were detected as uniform premature ventricular ectopics in 15%, multiform ventricular ectopics in 60%, and ventricular tachycardia in 30% of the cases. Four of our patients sustained repeated episodes of ventricular tachycardia. We concluded that the more malignant the arrhythmia, the higher mortality risk in such patients.

Impaired ventricular contractile function with dilatation of either or both ventricles is the common presentation of dilated idiopathic cardiomyopathy.[1] Sudden and unexpected death is common among patients with idiopathic dilated cardiomyopathy, and probably results from various types of arrhythmias.[2] In dilated cardiomyopathy, cardiac arrhythmias are frequent and severe, may co-exist with heart failure, and are considered a cause of cardiac arrest.[2,3] Huang et al[4] in 1983 and Unverferth et al in 1984 concluded that the prognostic value of these arrhythmias is unclear.[4,5] Caplan and Fuster,[6] in a 1985 report that assessed the natural history of idiopathic dilated cardiomyopathy, stated that patients can be evaluated for risk factors of mortality through quantitative assessment of their arrhythmias.

Long-term ambulatory electrocardiographic monitoring has been useful in diagnosing various types of arrhythmias and evaluating their significance in different cardiac disorders. In idiopathic dilated cardiomyopathy, the prevalence of arrhythmias detected by long-term ambulatory Holter monitoring has not been evaluated fully, and their clinical significance and prognostic value are still unclear.

Since idiopathic cardiomyopathy remains a challenge because of its ill-defined natural history and its generally unsatisfactory response to therapy, there is an urgent need for understanding this fatal disease. With early recognition of the potentially lethal arrhythmias that complicate the disease, patients may benefit from new therapeutic advances.

Patients and Methods

Sixty consecutive patients with idiopathic dilated cardiomyopathy were included in this

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study. Diagnosis was based on clinical findings according to the criteria of Fuster et al.[7] There were 33 males (55%) and 27 females (45%). Mean age was 24.6 and 38 years, respectively. The diagnosis of idiopathic cardiomyopathy was confirmed by cross-sectional echocardiography according to the recommendation of Goldberg et al.[8] Interpretation of electrocardiograms, chest x-ray studies, and echocardiograms was performed independently by the two investigators. Ambulatory 24-hour Holter monitoring was performed in all patients using a Del Mar Avionics Model 900A machine. Results were analyzed independently by the two investigators. Patients were followed for six months under close clinical observation, along with serial electrocardiograms.

Results

The presenting symptoms or electrocardiographic findings in the patients at entry into the study indicated: congestive heart failure in 24 cases (40%), palpitations in 20 cases (33%), ventricular tachycardia in six cases (10%), and atrial fibrillation in 14 cases (23.3%).

Holter monitoring revealed the following supraventricular arrhythmias: chronic atrial fibrillation in 14 cases (23.3%), atrial extrasystoles in 18 cases (30%), and paroxysmal supraventricular tachycardia in 24 cases (40%).

The following ventricular arrhythmias were detected: unifocal premature ventricular complexes in nine cases (15%) and multifocal ectopics in 36 cases (60%). Episodes of ventricular tachycardia were recorded in 18 patients (30%), of which six cases (33.3%) had more than one episode.

By the end of the six-month follow-up, sustained ventricular tachycardia had developed in four patients (7%) who died despite efforts at resuscitation.

Discussion

The variable socioeconomic standards and multiracial population in the Kingdom of Saudi Arabia are factors that may affect the incidence of cardiovascular disorders. Dilated cardiomyopathy is a frequent heart disorder in this area[9] that continues to demand the attention of investigators and the practicing cardiologists. Twenty-four-hour electrocardiographic monitoring has documented cardiac arrhythmias as a cause of morbidity and mortality, and has found widespread application as a means of quantifying ventricular as well as supraventricular ectopy and guiding antiarrhythmic therapy.[10] Survival in patients with dilated cardiomyopathy has been related to clinical characteristics, hemodynamics, and ventricular function,[11] whereas the natural history as well as prognostic value of co-existing arrhythmias remain controversial.[12]

Costanzo-Nordin et al[13] indicated that the natural history of dilated cardiomyopathy is variable and the prognosis difficult to predict. They proposed several clinical and hemodynamic criteria as prognostic indicators and concluded that the relationship between arrhythmias, degree of hemodynamic impairment, and sudden death is controversial. Unverferth and co-workers[5] considered ventricular arrhythmia the second most important factor in the prognosis of dilated cardiomyopathy in which multiform premature ventricular complexes were related to poor prognosis. They also judged atrial fibrillation to be a significant risk factor, whereas Convert et al[14] felt that the presence of atrial fibrillation actually improved prognosis.

The data obtained from the present study are consistent with the hypothesis that complex ventricular arrhythmias are among the predisposing factors for cardiac death in patients with severe idiopathic dilated cardiomyopathy, as four patients died because of repeated episodes of ventricular tachycardia, and this agrees with the findings reported by Holmes et al.[15] This differed in the study done by Hamby[16] who found the prognosis was more closely related to the extent of failure than to complex arrhythmias. Missri[17] stated that the progression of dilated idiopathic cardiomyopathy is difficult to predict, as the median survival is usually less than five years. Investigations that included other invasive studies have shown that cases in which there are thick left ventricular walls and a large myocardial mass carry a more favorable prognosis.[18]

Unverferth et al[5] stressed that arrhythmias complicating idiopathic dilated cardiomyopathy represent an important prognostic factor. These workers recognized the direct correlation between the increased severity of arrhythmias and increased mortality. Therefore, our four patients with sustained ventricular tachycardia resulting in death are evidence that complex arrhythmias represent an independent risk factor in the presence of severe dilated cardiomyopathy.

The present study confirms that episodes of various categories of ventricular arrhythmias, detected by 24-hour Holter monitoring, even in combination with infrequent paroxysms of ventricular tachycardia, can carry considerable risk of sudden death.

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ACUTE PANCREATITIS: EXPERIENCE IN A UNIVERSITY HOSPITAL IN RIYADH, SAUDI ARABIA

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أجريت دراسة مراجعة على جميع حالات المرضى ممن يعانون من إلتهاب المعثكلة الحاد والذين أدخلوا تباعا إلى المستشفى الجامعي بالرياض على مدى خمس سنوات من ١٩٨٤م إلى ١٩٨٨م. كان إجمالي هجمات المرض ١٠٤ في ٩١ مريضًا. كان متوسط عمر المرضى ٤٤ر٤ عامًا ونسبة الإناث إلى الذكور ١ر٥ إلى ١. بلغت نسبة الحصاة الصفراوية المسببة للداء ٦٧٪ ، تم تشخيص حالة إلتهاب المعثكلة الحاد مجهول السبب في نسبة ١١ر٥٪ فقط. وفي مجموعة المرضى السعوديين الخمسين (٥٥٪) ، شكلت الإناث نسبة الثلثين وكان السبب لدى ٧٦٪ منهن إلتهاب المعثكلة المراري. وتبين باستخدام معيار جلاسجو المعدل لقياس شدة الداء، تصنيف ٢١٪ من الهجمات على أساس «داء شديد». بلغت نسبة الوفيات في هذه الحالات ٣ر٣٪، وحدثت جميع الوفيات في فئة «الداء الشديد» وكان جميعهم ممن يعانون من إلتهاب المعثكلة الحاد غير المراري. تطورت حالة ستة من المرضى إلى حدوث الكيسات الكاذبة، بما في ذلك خراج بنكرياسي في حالة واحدة. تشير هذه الدراسة إلى أن إلتهاب المعثكلة الحاد ليس من الحالات الشائعة بين الطوارىء الصحية في المملكة العربية السعودية وأنه غالباً ما يكون مرتبطاً بالمرارة، ويصيب الإناث على وجه الخصوص. يبدو أن الداء يتخذ مسارًا أكثر اعتدالاً وأن معدلات انتشاره ووفياته تقل عمّا يقابلها في الأقطار الغربية.

In a retrospective study, all cases of patients with acute pancreatitis admitted consecutively to the University Hospitals in Riyadh over the five-year period 1984-1988 were analyzed. There were a total of 104 attacks in 91 patients. Mean patient age was 42.4 years and the female to male ratio was 1.5:1. In 67%, gallstones were the associated cause; idiopathic acute pancreatitis was diagnosed in only 11.5%. Among the 50 (55%) Saudi nationals, two thirds were females and 76% had biliary pancreatitis. Using modified Glasgow severity prediction criteria, 21% of the attacks were designated as "severe disease." Mortality in this series was 3.3%; all deaths occurred in the "severe disease" group and all had nonbiliary acute pancreatitis. Pseudocysts developed in six patients, including a pancreatic abscess in one. This study shows that acute pancreatitis is not a common medical emergency in Saudi Arabia and is predominantly biliary-associated, especially affecting females. The disease seems to follow a more benign course and has lower morbidity and mortality than that described from the West.

The incidence of acute pancreatitis (AP) in western countries is increasing as its most common etiological associations, i.e., alcohol abuse and gallstones, are becoming more prevalent. AP exhibits a wide spectrum of severity, complications, and outcome. There is also a wide geographical variation in the incidence of the disease and its etiological associations.

Apart from two recent reports from Kuwait,[1,2] little is known about the disease for Arab Middle Eastern countries. We report our experience with AP at the University Hospitals in Riyadh, in an attempt to characterize the clinical pattern of the disease.

Patients and Methods

The case records of all consecutive patients with a computer-indexed diagnosis of AP seen during

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the five-year period 1404-1408H (1984-1988G) were analyzed retrospectively. All patients had been treated at the University Hospitals in Riyadh. Only patients with an elevated serum amylase on admission of at least 2.5 μkat/L (reference range, 0.38-1.41 μkat/L; Du Pont Automatic Clinical Analyzer) and a consistent clinical picture were included.

Information regarding age, sex, and nationality was extracted from the case record, and clinical and biochemical data on the course and outcome of the attack were studied, including management. Laboratory data were analyzed in relation to severity of the attack using modified Glasgow criteria.[3] The attack was considered severe if three or more of the following features were present in the first 48 hours after admission: age, > 55 years; white cell count, > 15 × 10^9/L; blood glucose, > 10 mmol/L (patients with diabetes mellitus not included); urea, > 16 mmol/L; arterial oxygen tension, < 60 mm Hg/L; albumin, < 32 g/L; calcium, < 2.0 mmol/L; and aspartate aminotransferase, 1.68 μkat/L. Diagnosis of biliary pancreatitis was based on the above criteria in the presence of biliary stones, as demonstrated by ultrasonography.

Results

Over the five-year period, 104 attacks of AP in 91 patients fulfilled the diagnostic criteria. This represents 0.1% of the total annual admissions to the University Hospitals in Riyadh. Eight patients had repeated admissions (range, 2-6). The female to male ratio was 1.5:1 and mean patient age was 42.4 years (range, 16-74). The age distribution is shown in Figure 1.

In 70 (67%) of the attacks, the underlying cause was biliary disease. Alcohol abuse was found in only seven patients (7.6%). Twelve patients (13%) had AP of unknown cause, and ten were males. Table 1 summarizes the associated causes of AP.

Fifty (55%) of the patients were Saudi nationals and two thirds of them were female. The etiological associations of AP in this subgroup are shown in Table 2.

The mean ± SEM serum amylase value at admission for all attacks was 25.72 ± 1.93 μkat/L (N = 100). Biliary-related cases of AP were associated with a higher amylase value than nonbiliary cases (Figure 2). In four attacks, the serum amylase was less than 2.5 μkat/L. One patient was

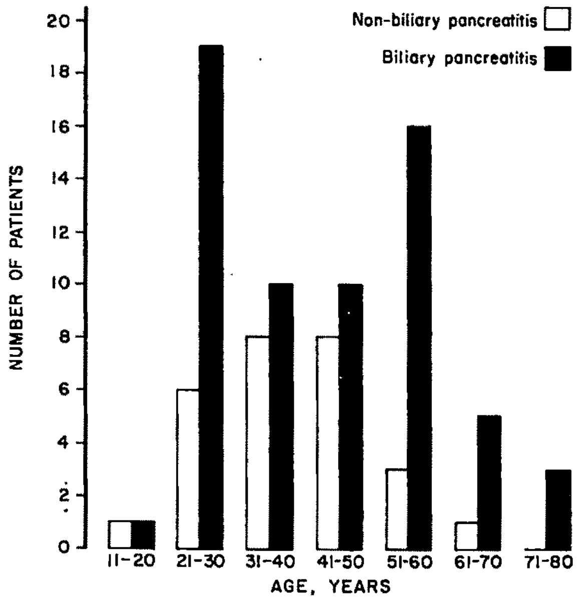

FIGURE 1. Age distribution among patients with biliary and nonbiliary pancreatitis (N = 91).

TABLE 1. *Etiological associations of acute pancreatitis in 104 attacks.*

Etiology	Male	Female	Total
Biliary	17	53	70(67.3%)
Alcohol	7	–	7(6.7)%)
Idiopathic (unknown)	10	2	12(11.5%)
Miscellaneous	11	4	15(14.4%)
Hyperlipidemia	6	1	7
Drug-induced	2	1	3
Trauma	1	1	2
Uremic	2	–	2
Postoperative	–	1	1

TABLE 2. *Etiological associations of 57 acute pancreatitis attacks in Saudi patients.*

Etiology	Male	Female	Total
Biliary	8	33	41(72%)
Alcohol	6	–	6(10.5%)
Idiopathic (unknown)	5	1	6(10.5%)
Uremic	2	–	2(3.5%)
Hyperlipidemia	–	1	1(1.8%)
Postoperative	–	1	1(1.8%)

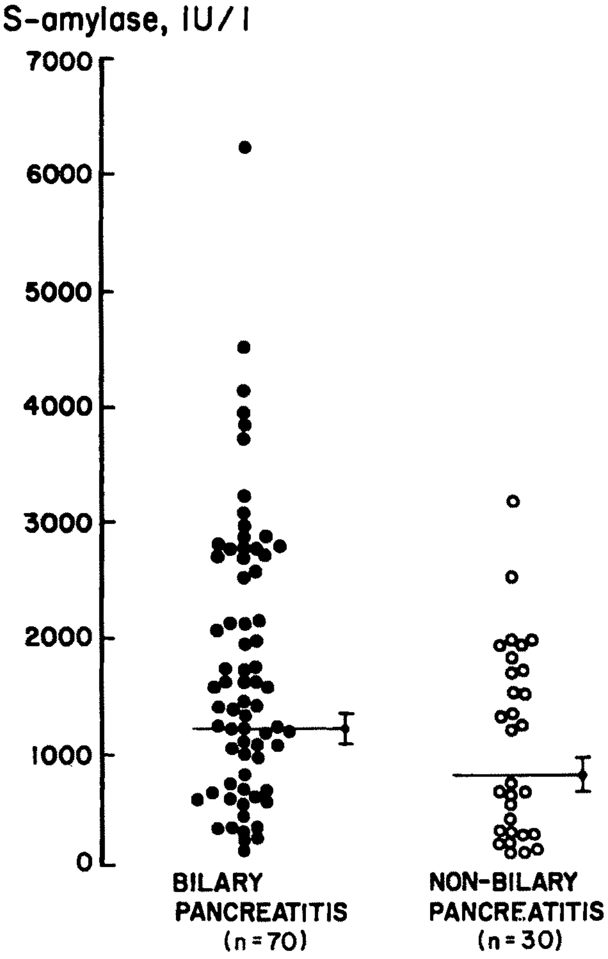

FIGURE 2. Serum amylase activity on admission for each patient with biliary and nonbiliary pancreatitis. (Mean value ± SEM is shown for each group.)

TABLE 3. *Details of fatal acute pancreatitis attacks.*

Case	Sex	Age(yr)	Etiology	Cause of death
1	M	42	Alcohol	Septicemia/ARDS/ shock
2	M	54	Idiopathic	ARDS
3	F	65	Postoperative	Septicemia/renal failure

ARDS = adult respiratory distress syndrome.

seen who had had acute abdominal symptoms for two days and admission serum amylase was 1.45 μkat/L. Emergency diagnostic laparotomy revealed acute hemorrhagic necrotizing pancreatitis, and amylase content in the ascitic fluid was found to be 39.0 μkat/L. The second patient had alcohol-associated acute relapsing pancreatitis and this patient was seen eight days after symptoms of AP started with an admission serum amylase value of 1.30 μkat/L. However, the urinary amylase value was diagnostic and plain abdominal radiograph showed pancreatic calcification. The third patient had recurrent pancreatitis associated with an old blunt injury. This patient was seen two days after the start of AP symptoms and serum amylase at admission was 0.63 μkat/L. Endoscopic retrograde cholangiopancreatography (ERCP) demonstrated a pseudocyst in the pancreas. The fourth patient had hyperlipidemia-associated acute relapsing pancreatitis and at recurrence had an amylase value of 1.23 μkat/L in grossly lipemic serum.

According to the modified Glasgow scoring criteria, 22 (21%) of the 104 attacks of AP were severe, with a mean score of 4 out of a possible 8 (range, 3-6).

Pancreatic pseudocysts (4-9 cm in diameter) were found in six patients, and one also had a pancreatic abscess. All six patients were treated surgically. Cholecystectomy was also done in 24 patients during their hospitalization for AP. Three patients died, giving a hospital mortality rate of 3.3%. Mean age in these patients was 54 years and all had necrotizing hemorrhagic pancreatitis rated as severe according to the Glasgow scoring criteria. Mortality among this subgroup was 14%. Details of these three fatal cases of AP are given in Table 3. The remaining 58 patients made a good recovery on conventional conservative treatment. Most of the patients were cared for on general medical wards.

Discussion

AP is a major medical problem in the West with an increasing incidence and carries a high morbidity and mortality. Serious complications occur in 20 to 30% of the cases, with death in 8 to 20%.[4-6] This five-year retrospective study of all the admissions for AP to the University Hospitals in Riyadh (> 600 beds) shows that AP is not a common clinical entity in Saudi Arabia, forming a small proportion of the total number of annual hospital admissions. This finding should be representative of the incidence in major hospitals in the Kingdom, as the University Hospitals adopted an open-access policy during the study period and were accepting both Saudi nationals and expatriates with acute medical problems. Since there is no defined catchment population for these hospitals, it is difficult to extrapolate the incidence of the disease to the community as a whole.

Gallstones were the most common underlying cause of AP in the present series, especially among Saudi patients. In this subgroup, biliary pancreatitis constituted more than 70% of all the attacks. The female to male ratio was 4:1 and this agrees with the sex distribution seen among patients with gallstones who underwent cholecystectomy at one of the institutes in this study.[7] As expected, and in support of reports from Kuwait,[1,2] alcohol consumption, while it is the second most common etiological factor for the disease in the West, fares low in this series because of the religious, social, and legal constraints on alcohol use in Saudi Arabia. Drug intake was implicated in three of the patients: thiazide in one, a large dose of corticosteroids in another, and AP developed in the third patient after administration of glibenclamide for recently diagnosed type II diabetes mellitus.

Idiopathic AP was diagnosed in only 11.5% of the attacks. This is in sharp contrast with the 27% reported from the West[8] and the 37% reported recently from Kuwait.[2] The low percentage in our study could be partly explained by the high proportion of biliary-associated AP diagnosed by ultrasonography, which all of our patients with AP underwent shortly after admission.

Serum amylase activity of at least twice the upper limit of the reference interval, in the right clinical setting, is usually diagnostic of AP.[9,10] This was the case in all except four of the total 104 attacks studied. The alternative methods of diagnosing AP in these four cases have been described. Our findings support the use of serum amylase as a routine screening test for AP, though one should be aware of its shortcomings, such as in cases of late presentation or of hyperlipidemia as seen in a few of our patients. Other supportive tests such as urinary amylase or serum lipase activity and special imaging techniques could be used in such situations. Serum amylase activity tends to be higher and returns to normal earlier in biliary-associated AP, as observed in the present study. AP was diagnosed in only two patients (2.2%) at laparotomy compared with 5% quoted from the West.[11]

Serious complications of AP supervene in 20 to 30% of cases, with death in 8 to 20%.[4-6] The early differentiation of patients with mild and severe disease is important if prompt intensive management is to benefit those with severe disease. The criteria introduced by Ranson and modified by Imerie are now generally accepted as providing the best assessment of severity in AP.[8] One such modification was adopted in the present study,[3] with the exception that serum aspartate aminotransferase was substituted for lactate dehydrogenase. According to the index of severity adopted, 21% of the cases were severe, but with a low mean score of 4 out of a possible 8. The 3.3% mortality in the series is rather low, and all deaths occurred in patients with AP graded as severe, giving a 14% mortality in this subgroup. This again emphasizes the importance of early recognition of severe attacks. None of the deaths occurred in the patients with biliary-associated AP. The mortality from AP due to gallstones, however, has been reported to be around 10% in various series.[4,12,13] In a recent prospective study, Neoptolemos et al[14] found that ERCP and endoscopic sphincterotomy done in patients with severe AP due to gallstones was associated with lower morbidity and shorter hospital stays than were seen in patients who had conservative treatment. Early cholecystectomy has been advocated by some,[15] while others have concluded that urgent surgery is accompanied by increased mortality.[13,16,17]

In the present series, most patients were treated conservatively in medical wards. Emergency surgery was only required in eight patients, two for diagnostic laparotomies and six for pancreatic pseudocysts including an abscess. All cholecystectomies were performed well after resolution of the AP. ERCP was only performed in a few cases. There is a tendency to formalize the investigations and management of biliary pancreatitis at our institution, including ERCP with or without endoscopic sphincterotomy and early (not emergency) cholecystectomy as indicated.

AP does not seem to represent a major medical emergency in Saudi Arabia. Gallstones are the predominant associated factor, especially among Saudi nationals, the majority being females. The disease seems to follow a more benign course than that seen in the West, with lower mortality and morbidity. ERCP with or without endoscopic sphincterotomy, as advocated recently for severe cases, and early cholecystectomy after resolution of the attack during the same admission should be considered for the management of biliary-associated pancreatitis.[14,17]

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CHILDHOOD BACTERIAL MENINGITIS IN TABUK, SAUDI ARABIA

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عولج ٤٩ طفلاً من إلتهاب السحايا الجرثومي من بين ٥٤٥٤ طفلاً (٤٩, ٠٪) أدخلوا جناح طب الأطفال بمستشفى القوات المسلحة في تبوك خلال السنوات الست ما بين ١٩٨٢ - ١٩٨٧م. كانت أعمار تسعين بالمائة منهم تقل عن ٢٤ شهرًا. وعزلت العضويات المسببة فكانت كما يلي: **المستدمية النزلية من النمط ب** (٥٥٪)، **المستدمية النزلية** ٢٪، **العقدية الرئوية** (١٨٪) النيسرية السحائية (٢٪). ولم ينبت السائل النخاعي المزروع أية عضويات لدى ٢٢٪ من المرضى. وكان سن تسعة وثمانين بالمائة من الأطفال المصابين بإلتهاب السحايا بالنمط ب من المستدمية النزلية أصغر من ٢٤ شهرًا. كان خمسة وأربعون بالمائة من الأطفال قد سبق تناولهم علاجًا بالصادات. ظهرت المقاومة للامبيسلين لدى أحد عشر بالمائة من حالات إلتهاب السحايا بالمستدمية النزلية بالنمط ب والمقاومة للامبيسلين والكلور امفنكول معًا لدى سبعة بالمائة. وكانت النسبة الإجمالية للوفيات ٣, ١٤٪. توبعت حالات الناجين مدة لا تقل عن ٤ أشهر ولا تزيد عن ٩٦ شهرًا. وظهرت اختلاجات معاودة وتخلف نفسي حركي على ١٢٪ وكذلك إعاقة حسية عصبية لدى ٢٪ .

During the six-year period 1982 to 1987, 49 of 5454 children (0.89%) admitted to the pediatric medical ward of the Armed Forces Hospital in Tabuk were treated for bacterial meningitis. Ninety percent were younger than 24 months. The causative organisms isolated were *Hemophilus influenzae* type B (55%), *H. influenzae* (2%), *Streptococcus pneumoniae* (18%), and *Neisseria meningitidis* (2%). Cerebrospinal fluid cultured showed no organisms in 22% of the patients. Eighty-nine percent of the children with *H. influenzae* type B meningitis were younger than 24 months. Forty-five percent of the patients had had prior antibiotic treatment. Eleven percent of the cases of *H. influenzae* type B meningitis were ampicillin resistant, and 7% were both ampicillin and chloramphenicol resistant. The overall mortality was 14.3%. Survivors were followed from a minimum of 4 months to a maximum of 96 months. Recurrent seizures and psychomotor retardation were found in 12% and sensorineural impairment in 2%.

Bacterial meningitis is an acute illness that can occur at any age, and is associated with marked morbidity and mortality. Many patients who survive the disease have some residual neurological sequelae such as mental retardation, cranial nerve abnormalities, convulsions, and hydrocephalus.[1,2] Prompt diagnosis and aggressive management are important but early signs and symptoms of meningitis are often subtle and nonspecific, depending on the age of the child. Although the diagnostic methods are relatively simple and antimicrobial agents are effective, bacterial meningitis continues to cause deaths in children worldwide.[3,4]

There have been isolated studies of childhood bacterial meningitis in Saudi Arabia,[4,5] but no studies have come from the Northwestern region. This study documents the various clinical and bacteriological aspects of pyogenic meningitis during childhood, beyond the neonatal period, in the Northwestern region of Saudi Arabia.

Material and Methods

The medical records of all children treated for bacterial meningitis in the medical pediatric ward of the Armed Forces Hospital, Tabuk, were

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reviewed retrospectively for the six-year period, 1982 to 1987. The study population included all children who were past the neonatal period. Because of admission regulations of the hospital, the upper age limit was 12 years.

Information obtained from the records included patient age and sex, duration of illness and type of treatment before admission, complaints at presentation, and clinical symptoms and signs on admission. Laboratory findings from analysis of the cerebrospinal fluid (CSF), with particular reference to Gram staining, organisms cultured, and their sensitivity results, were also noted. Details of the various combinations of antimicrobial agents used in the treatment were not considered, as this is the subject of another ongoing study. Details of the hospital course, outcome, and follow-up of these patients were also recorded.

Results

Of a total of 5454 medical pediatric admissions during the 6-year period, 49 children (0.89%) were treated for bacterial meningitis. Diagnosis was based on findings from biochemical, microscopic, and microbiological examination of the CSF. Of the 49 children, 31 (63%) were males and 18 (37%) were females. Eighty-four percent of the children (N = 41) were below 12 months of age and 90% (N = 44) were below 24 months. The remaining five ranged in age from 2 to 5 years. With respect to the duration of the illness before presentation, medical help had been sought in 27 (55%) by the third day of the illness and in 32 (65%) by the fourth day. Although the disease occurs throughout the year, 29 of the cases (59%) occurred between September and December. There was a positive history of respiratory tract infection in five families. A positive history of serious illness in a sibling (meningococcemia) was elicited in only one patient's family.

Complaints at presentation are shown in Table 1. Fever (i.e., body temperature, preferably rectal, > 37.6°C) was the most common complaint (80%) and the three most prevalent complaints did not refer to the central nervous system. Conversely, manifestations such as convulsions, drowsiness, and nuchal rigidity were less common. However, the signs and symptoms noted at clinical examination were: fever (63%), neck stiffness (47%), bulging anterior fontanelle (27%), irritability (27%), and lethargy (20%). Twenty-two of the patients (45%) were treated with antimicrobial agents 24 to 48 hours before presentation. No organism was grown in the CSF of seven of these children.

TABLE 1. *Presenting complaints in children with bacterial meningitis.*

Complaints	No. of patients*
Fever	40(82)
Vomiting	22(45)
Diarrhea and vomiting	17(35)
Irritability	13(27)
Upper respiratory symptoms	9(18)
Convulsions	8(16)
Drowsiness	4(8)
Neck stiffness	4(8)

*Percentages in parentheses.

Causative organisms were cultured from the CSF in 38 of the 49 children (78%) while cultures in the remaining 11 children (22%) showed no organisms. Four of these 11 children had been treated in other hospitals before referral to our hospital. Organisms cultured from the CSF were: *Hemophilus influenzae* type B (HiB) (55%), *Streptococcus pneumoniae* (18%), *Neisseria meningitidis* (2%), and *Hemophilus parainfluenzae* (2%). Twenty-four of the 27 children (89%) with HiB meningitis and five of the nine children (66%) with *S. pneumoniae* meningitis were younger than 24 months. Gram-positive organisms were found in nine children (33%) with HiB infection and in four children (44%) with *S. pneumoniae* infection. Blood culture was positive in ten patients (37%) with HiB meningitis and in five patients (55%) with *S. pneumoniae* meningitis.

The HiB organism in three patients was beta-lactamase positive and therefore resistant to ampicillin (11%); in two patients the HiB was resistant to both ampicillin and chloramphenicol. No complications were encountered in 23 of the patients (47%). Complications encountered during hospitalization were: convulsions (24.5%), fever 8%, computed tomographic (CT) changes (14.3%), neurological deficits (6%), and shock

(2%). Seven patients (14.3%) died, for a total mortality of 14.3%. Convulsions were generalized in most cases and recurred in more than half during hospitalization. CT scan changes included subdural effusions of varying degree and slight dilatation of the ventricles. Neurological deficits observed during hospitalization included facial nerve palsy, hypotonia, and residual hemiplegia.

Follow-up records were available for all 42 survivors and follow-up ranged between four and 96 months. Of the 23 children without complications during hospitalization, only one showed psychomotor retardation during follow-up, but this child had shown prior psychomotor delay due to intrapartum asphyxia. Five patients (12%) had recurrent seizures and psychomotor retardation following discharge from the hospital; one (2%) had sensorineural hearing impairment. The occurrence of recurrent convulsions during hospitalization was prognostically unfavorable, especially when there was an accompanying neuroanatomical disorder, which was documented clinically or by CT scan.

Two of the children who had recurrent seizures during hospitalization, but no neuroanatomical disorders, remained well at follow-up. On the other hand, eight of the ten children with recurrent seizures during hospitalization, as well as neuroanatomical abnormalities which were documented clinically or by CT scan, had neurological and developmental deficits at follow-up.

Although bacterial meningitis represented 0.89% of the medical/pediatric admissions, the number of deaths (7 of 111) represented 6.3% of the total medical/pediatric deaths during that period.

Of the seven patients who died, four had HiB infection and one had *Neisseria meningitidis* infection. The CSF of the remaining two patients yielded no organisms. Four of the patients had been referred from other hospitals.

Discussion

Most cases of bacterial meningitis in children older than two months of age are due to HiB, *S. pneumoniae*, or *Neisseria meningitidis*.[5,7] HiB was the most common organism in our series, accounting for 55% of the cases, while *S. pneumoniae* was found in 18% and *Neisseria meningitidis* in 2%. Corresponding figures from the Eastern Province of Saudi Arabia were 42%, 24%, and 11%, respectively.[5] The lower incidence of *Neisseria meningitidis* seen in our series contrasts with 11% from the Eastern Provinces and 30% from Switzerland.[8] This is probably the consequence of immunization with *Neisseria meningitidis* vaccine, which has been done in our region for some years.

There were more males than females in our series, confirming the generally observed male preponderance. Most patients (90%) were below the age of 24 months, also confirming the findings of others.[5,9] Twenty-four of our 27 children (89%) with HiB meningitis were younger than 12 months.

Of the physical signs observed at initial examination, some did not correspond to the symptoms described at admission. Fever was the only dominant symptom. Whereas manifestations such as nuchal rigidity, bulging anterior fontanelles, and seizures, which would alert one to a disease of the central nervous system, were less often noted, the physical signs were obvious on physical examination. It is of course conceded that some parents may not observe these physical signs even when they are present. This emphasizes the nonspecific nature of the usual initial complaints.

Forty-five percent of our patients were treated with antimicrobial agents before admission to our hospital. Even when children receive antibiotic drugs intravenously for 44 to 48 hours, the infecting organism can be detected chemically and morphologically in most cases.[10] When children with HiB meningitis are given oral antibiotic agents, subsequent CSF cultures will generally grow the organism, but this is not the case for pneumococcal and meningococcal disease.[10]

Careful examination of the Gram stain of the CSF is crucial, and organisms can be seen in centrifuged samples in 89 to 90% of patients who have positive bacterial culture,[11] but the specificity of the Gram stain decreases in patients who have had antimicrobial therapy.[12] This probably accounts for the low yield with Gram stain noted in our patients, 45% of whom had had prior antimicrobial treatment.

Isolation and identification of the causative agent from the CSF and blood can assist in the selection of the best antimicrobial therapy for the patient. The emergence of beta-lactamase-producing, and therefore ampicillin-resistant, strains of HiB[5,9,13,14] or ampicillin- and chloramphenicol-resistant strains[4,7,9,13,15,16] makes such tests mandatory. Eleven percent of our cases of HiB infection were resistant to both ampicillin and chloramphenicol. Corresponding figures from the Eastern Province were 14% and 2.3%, respectively.[5]

The resistance of HiB to both ampicillin and chloramphenicol in 7% of our cases is cause for concern. These two agents are used frequently in the initial treatment of pyogenic meningitis. Therefore the susceptibility of the identified organisms to the antimicrobial agents prescribed should be determined. Documentation of any resistant isolates warrants determination of the minimum inhibitory concentration of these isolates. We could not confirm whether this was done in our patients.

The use of the third-generation cephalosporins is recommended in these multiple-resistant strains of HiB,[3,8,15] but we do not think third-generation cephalosporins are warranted as first-line drugs in children who are older than two years in our area of Saudi Arabia.

Our mortality rate of 14.3% compares with the 15.2% observed in the Eastern Province,[5] and four of the deaths were in children who had been treated in other hospitals before referral to ours.

The most common problem among our survivors was recurrent generalized seizures, combined with psychomotor retardation in 12% of the cases. Sensorineural hearing impairment occurred in 2%, detected by evoked response audiometry. No sophisticated psychomotor studies were carried out, because of inadequate staff, but all affected children were functioning at a much lower level than their immediate younger siblings, especially in their verbal performance.

Despite early diagnosis, prompt initial treatment, and use of newer generation antimicrobial agents, bacterial meningitis continues to cause significant mortality and morbidity.[7] In fact, fatality rates have not changed appreciably in the past two decades.[7] Prevention, through administration of vaccines, is therefore the most desirable route in dealing with meningitis. Since about 90% of the children who had HiB meningitis in this series were below 2 years of age, the vaccine that is currently given to children over 2 years of age in the U.S. may not be of much value to Saudi children in the Northwest provinces. It is of continuing importance for physicians to maintain a high index of suspicion for meningitis when confronted with febrile pediatric patients.

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COAGULATION PARAMETERS IN MATERNAL AND CORD BLOOD AT DELIVERY

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درسنا مجموعة واسعة من المتغيرات المتعلقة بالارقاء لدى ٣٠٠ أم ووليدها إبّانْ ولادته وكذلك لدى ٣٧٥ حالة لنساء غير حاملات وبحالة صحية جيدة واللاتي شكلن مجموعة الضبط.

وجد تطاول هام في زمن البروثرمبين، وزمن الثرومبوبلاستين الجزئي وزمن الربتليز في دم الوليد (السرى) مقارنة بدم الأم. كانت مستويات الفيبرينوجن في البلازما، وكذلك مضاد الثرومبين الثالث، والبروتين ج، والبلازمينوجن، ومخثر العامل الثامن وأنشطة تميم العامل ريستوستين، والعامل العاشر، وعدد الصفيحات الدموية منخفضة بدرجة ملحوظة في المواليد عن مثيلاتها في بلازما الأمهات. وعلى خلاف ذلك، فإن زمن الثرومبين، ومضاد بلازمين ـ ألفا ٢، ونواتج تدرك فبرين البلازما قد أشارت إلى قيم متقاربة في كل من الأمهات والمواليد. أظهر مستضد عامل فون ويلبراند ارتفاعا ملحوظا بدرجة كبيرة في الأمهات عن المواليد، في حين أن نسبة مستضد عامل فون ويلبراند ومخثر العامل الثامن كانا متشابهين في الأمهات والمواليد (١,٥٦ و١,٥٧ على التوالي).

لوحظ ترابط مهم فقط بين مستويات مخثر العامل الثامن لدى الأمهات ومواليدهن ($r = 0.69; P < 0.05$) في حين لم نجد ترابطا بين متغيرات الأرقاء الأخرى التي تمت دراستها. ونناقش هنا الاختلافات بين النتائج التي توصلنا إليها والتقارير المنشورة من دراسات أصغر حجما.

A wide range of hemostatic variables were studied in 300 maternal/neonatal pairs at the time of delivery and also in 375 healthy nonpregnant women who served as controls. There was significant prolongation of the prothrombin time, partial thromboplastin time, and reptilase time in neonatal (cord) blood compared to maternal blood. The plasma levels of fibrinogen, antithrombin III, protein C, plasminogen, factor VIII coagulant and ristocetin cofactor activities, factor X, and platelet counts were significantly lower in neonatal than maternal plasma. In contrast, the thrombin time, alpha2-antiplasmin, and serum fibrin degradation products showed comparable values for both mothers and neonates. von Willebrand factor antigen showed a more significant elevation in mothers than neonates; however, the ratio of von Willebrand factor antigen/factor VIII coagulant was similar in both (1.56 and 1.57, respectively). There was a significant correlation only between factor VIII coagulant levels in mothers and their babies ($r = 0.69$; $P < 0.05$) but not for the other hemostatic variables studied. The differences between our results and those reported in smaller published studies are discussed.

The newborn period is characterized by low levels of the measured components of the hemostatic system compared to adult values.[1-16] Although this subject has interested many researchers in the last two decades, the numerous data available for healthy newborn infants are inconsistent and difficult to obtain and interpret. This is due to such factors as variable methods of blood collection and assay procedures, variable gestational age,

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birth weight and vitamin K status, wide ranges of clotting factor proteins, and small number of observations, which make it difficult to define true normal values or to draw valid comparisons between these data.[2,7]

Most of the data published on this subject are based on findings in Caucasians and cannot necessarily be applied to Arabs, in view of the well-established ethnic group differences in hemostatic variables believed to underlie the varying incidence of thrombosis and hemorrhage in different populations.[17-19]

The purpose of this study, which is an offshoot of a population-based study of hemostatic variables in Saudi Arabia, is to determine the normal values for various plasma coagulation and fibrinolytic variables in full-term healthy Saudi neonates and their mothers at the time of delivery.

Subjects and Methods

Blood samples were collected randomly from 300 Saudi mothers and their babies at the time of delivery. All mothers were healthy and had normal full-term (37 to 42 weeks) pregnancy, labor, and uneventful delivery at the Riyadh Maternity Hospital. Their age range was 16 to 45 years (mean, 26.1; SD, 5.8). Their last recorded weights before delivery ranged from 40.5 to 121 kg (mean, 66.3; SD, 13.5), and their heights ranged from 140 to 199 cm (mean, 154.6; SD, 6.8). Newborn weights ranged from 2.5 to 5 kg (mean, 3.27; SD, 0.5). Babies with weights of 2.5 kg or less were excluded to avoid the possibility of diseases which affect low-birth-weight infants. Mothers were not under any form of drug therapy until they went into labor. This study is part of a population based survey of hemostatic variables in healthy Saudis, and the results obtained in nonpregnant women of childbearing age (N = 375) were used as controls. The ages of the control subjects ranged from 12 to 50 years (mean, ± SD, 25.8 ± 12.2).

Blood Sampling

Immediately after delivery of the baby, the cord was clamped. Before the placenta was delivered, blood for coagulation assays was drawn from the umbilical vein into syringes containing 0.1 M sodium citrate (Monovette; Sarsdt, West Germany) to yield a final ratio of nine parts blood to one part citrate. In addition, blood for platelet counts was collected in EDTA tubes. Maternal blood was drawn in the same manner from a vein in the antecubital fossa. The same nurse collected all blood samples, which were kept in melting ice and taken immediately to the laboratory. Platelet-poor plasma was prepared by centrifuging the sample at 1500 *g* for 15 minutes in a refrigerated centrifuge (4-6°C) (Beckman Model J-6B). Aliquots of plasma were stored at -40°C until analysis at a later date.

The following hemostatic tests were performed as described previously,[20,21] unless otherwise indicated: prothrombin time (PT), partial thromboplastin time (PTT), thrombin time (TT), reptilase time, plasma fibrinogen, antithrombin III, ristocetin cofactor, serum fibrin degradation products (FDPs); von Willebrand factor antigen (vWFAg) by a modification of Laurell's technique,[22] and platelet counts by a thrombocounter (Coulter Electronics). The following parameters were assayed by chromogenic substrates according to instructions of the manufacturers: plasminogen and alpha2-antiplasmin (Berichrome Kits; Behring, West Germany), factor VIII coagulant (factor VIII:C), and factor X and protein C (Coatest Kits; Kabi, Sweden). Normal pooled plasma used as control for these coagulation assays was obtained from no less than 20 healthy volunteers and was taken to represent 100% activity of the various assays. These volunteers were all Saudi blood donors, aged 21 to 45 years (mean ± SD, 29.5 ± 6.9).

Statistical Methods

The maternal versus neonatal data were evaluated and tested for significance. Using the pairs of results (i.e., mother and baby), the paired Student's *t* test (two-tailed) was used to test for the significance of the mean difference between maternal and neonatal results. The unpaired *t* test was also used to compare maternal and neonatal data with control data.

Results

There was significant prolongation of the PT, PTT, and reptilase time in cord blood compared with maternal and control blood. Likewise the plasma levels of fibrinogen, antithrombin III, clotting factor VIII:C, ristocetin cofactor, vWFAg, protein C, and plasminogen were significantly lower in cord plasma than in maternal and control plasma. Conversely, platelet counts and packed cell volume were higher in cord than maternal blood, while thrombin times, alpha2-antiplasmin, and serum FDPs were of similar magnitude in both. Alpha2-antiplasmin content was significantly lower in neonates and mothers compared with controls.

The vWFAg exhibited a more marked elevation in maternal than neonatal blood; however, the ratio of the antigen to factor VIII:C was the same magnitude in both maternal and neonatal blood (1.56 and 1.57, respectively). These levels were significantly higher than control values. Analysis of variance showed significant correlation between the factor VIII:C levels in mothers and their babies ($r = 0.69$, $P > 0.05$) but not in other hemostatic variables. Table 1 provides a summary of these variables.

Discussion

Uncontrolled bleeding and thromboembolic disorders during childbirth remain a major cause of maternal and neonatal morbidity and mortality.[23,24] While the factors that predispose to these anomalies remain obscure, derangement of the hemostatic system is a prime feature of these disorders and a major target for therapeutic interventions. Normal reference levels for hemostatic variables are needed for both maternal and neonatal blood in the presence of a normal uneventful delivery, so that disorders of hemostasis can be detected.

The data obtained in the present study confirm

TABLE 1. *Results of hemostatic variables in maternal/neonatal pairs and nonpregnant adult controls.*

						P values		
Variables	N	Mothers X ± SD	Neonates X ± SD	N	Controls X ± SD	Mothers vs neonates	Mothers vs control	Neonates vs control
PT (sec)	282	11.3 ± 0.9	12.9 ± 2.9	375	11.8 ± 0.9	§	§	§
PTT (sec)	279	29.4 ± 3.8	39.9 ± 7.7	375	26.8 ± 2.8	§	§	§
TT (sec)	307	15.4 ± 3.2	15.4 ± 4.2	365	16.7 ± 3.1	NS	NS	NS
RT (sec)	263	13.2 ± 1.6	19.9 ± 3.4	294	11.9 ± 1.1	§	§	§
FIB (mg/dL)	233	482.9 ± 119.8	172.6 ± 64.2	281	309.1 ± 74.5	§	§	§
ATIII (%)	219	86.1 ± 14.4	48.1 ± 12.7	234	103.5 ± 12.1	§	§	§
Ristocetin cofactor (%)	49	214.8 ± 96.6	128.6 ± 66.4	103	111.8 ± 35.0	‡	§	*
Factor X (%)	143	129.3 ± 17.4	49.1 ± 9.7	51	112.8 ± 213.0	§	§	*
PLTCNT $(\times 10^3/\text{mm}^3)$	258	241.4 ± 89.2	272.2 ± 101.8	274	277.8 ± 66.5	‡	§	NS
PCV (%)	264	38.0 ± 4.1	48.6 ± 5.9	214	40.2 ± 3.2	§	§	§
Plasminogen (%)	99	102.1 ± 16.8	48.2 ± 13.2	176	112 ± 15.0	§	§	§
Alpha2-antiplasmin (%)	77	83.8 ± 15.0	81.9 ± 21.6	176	98.6 ± 13.3	NS	§	§
FDP (μg/mL)	74	14.4 ± 9.9	15.5 ± 11.1	–	—	NS	–	–
vW antigen	37	402.0 ± 177.6	146.7 ± 50.6	151	111.1 ± 46.3	§	‡	*
FVIII:C	37	257.6 ± 98.4	93.3 ± 41.2	151	110.3 ± 60.2	§	§	NS
vW antigen/ FVIII:C	37	1.56	1.57	151	1.0	NS	*	*
Protein C	39	95.9 ± 27.3	29.9 ± 10.2	37	110.1 ± 29.3	§	NS	§

* $P < 0.05$; † $P < 0.01$; ‡ $P < 0.005$; § $P < 0.001$; – = not done.
PT = prothrombin time; PTT = partial thromboplastin time; TT = thrombin time; RT = reptilase time; FIB = fibrinogen; ATIII = antithrombin III; PLTCNT = platelet count; PCV = packed cell volume; FDP = fibrin degradation products; vW = von Willebrand; FVIII:C = factor VIII coagulation; NS = not significant.

TABLE 2. *Normal values of variables in healthy full-term neonates as reported in the literature.**

Report	PT (sec)	PTT (sec)	TT (sec)	RT (sec)	FIB (mg/dL)	ATIII (%)	FVIII:C (%)	F:VIII RICOF (%)	F:VIII R:Ag (%)	FX (%)
Hathaway & Bonnar[1]	14.5 (13–17)	71 (APTT)	15	16 (21–35)	215 ±35 (14–18)	60 ±16	97	(50–180)	–	–
Weibbach et al[2]	–	70.2	31.2	–	253	87.3	–	–	–	40.8
Glader et al[3] (N=75)	14–22	35.55	–	–	150–300	–	–	–	–	–
Jurgens et al[7] (N = 33)	–	–	17.8 ± 9.1	–	218 ± 57	57.2 ± 13.1	–	–	–	–
Buchanan[5]	12–16	30–45	–	–	200–400	–	–	–	–	–
Stuart et al[6]	12.9 ± 18	64.9 ± 12.1	30.3 ± 3.8	–	–	–	–	–	–	–
Andrew et al[7] (N = 61)	13 ± 1.4	42.9 ± 5.8 (APTT)	23.5 ± 2.4	–	283 ± 0.6	63 ± 12	100 ± 39	153 ± 67	–	40 ± 14
Barnard et al[11] (N = 24)	13.6 12.8–14	65.2 50–84 (APTT)	12.5 10–15	–	246 (200–320)	56 (32–111)	–	–	–	–
Preston[8] (N = 27)	–	–	–	–	–	–	100.5 (66–190)	–	–	–
Kries et al[9] (N = 60)	–	–	–	–	–	–	127 ± 55 (54–300)	–	136 ± 37 (64–292)	–
Johnson et al[10] (N = 30)	–	–	–	–	–	–	148 ± 53 (55–288)	148 ± 55 (88–282)	134 ± 54 (52–288)	–
Present study	12.9 ± 2.9	39.9 ± 7.7	15.4 ± 4.2	19.9 ± 3.4	172.6 ± 64.2	48.1 ± 12.7	93.3 ± 41.2	128.6 ± 66.4	146.7±50.6	49.1±9.7

*Most values are expressed as the mean ± standard deviation. Others are expressed as ranges. RICOF = ristocetin cofactor; FVIII:R:Ag = factor VIII-related antigen; FX = factor X; PROT.C = protein C; PLG = plasminogen; AP = alpha2-antiplasmin; APTT = activated PTT. All other abbreviations as in Table 1.

the differences that have been established between cord blood and venous maternal or adult blood.[1-16] The data, which represent the reference values for Saudi neonates, are compared in Table 2 with similar data from other ethnic populations.

The reference values obtained for the routine coagulation screening tests (i.e., PT, PTT, reptilase time, plasma fibrinogen, and platelet counts) agree, to a great extent, with both the published mean values and population ranges in Caucasians, and indicate a significant diminution in the coagulation mechanism in the newborn.

The thrombin time produced an unexpected similar range and mean values for mothers and neonates, and this could be due to reasons inherent in the technique. The thrombin time was measured by mixing calcium chloride with thrombin before adding the mixture to citrated plasma. Our data confirm the recent findings of Andrew et al[7] but disagree with many earlier reports of prolonged thrombin time in neonates.[1,2,4,6,7,11] Andrew et al[7] ascribed their results to the addition of calcium ions to the buffer used in the test, an observation that was reported earlier.[25]

On the other hand, the reptilase time, which has been determined in few previous investigations,[1] was significantly prolonged in the neonates in our study. Such prolongation, in the absence of significantly elevated fibrin degradation products, is indicative of defective fibrin polymerization (dysfibrinogenemia).[25] This is not unexpected since fetal fibrinogen is qualitatively different from adult fibrinogen.[26]

The previously reported values for the activated partial thromboplastin time in the neonate were so prolonged (Table 2) that the usefulness of the test in infants has been questioned.[27] We used an activated PTT reagent that yields reasonably short clotting times and considerably narrow maternal and neonatal ranges. Prolongation of the PTT in the neonate is attributed to a deficiency of the clotting factors operating in the intrinsic pathway of the clotting system.[7,11,27-29] This in turn is due to immature synthetic capabilities of the liver rather

PROT C (%)	PLG (%)	AP (%)	FDP (μg/mL)	PLTCNT (×10³/mm³)
–	43 ± 16	–	0–16	310 ± 68
–	54.2	70.5	24.9 ± 5.0	244.9
–	–	–	–	150–400
–	–	87.1 ± 13.7	–	–
–	–	–	10	150–400
–	–	–	–	362 ± 84
0.35 ± 9	(50%)	85 ± 15	–	–
–	–	–	4.25	250 (150–350)
–	–	–	–	–
–	–	–	–	–
–	–	–	–	–
29.9± 10.2	48.2±13.2	81.9±21.6	15.5±11.1	272±101.8

than vitamin K deficiency.[1,3,13,28,29]

Previous studies on the levels of factor VIII activities (factor VIII:C, vWFAg, and ristocetin cofactor) in the newborn have yielded widely contrasting results. While some authors have found neonatal factor VIII:C levels to be within the normal adult range,[7,12] others have found factor VIII:C and vWFAg to show higher values in newborns than adults.[9] We found factor VIII:C levels in neonates were at the lower end of the adult normal range, but the calculated mean is significantly lower in neonates than adults. However, our findings showed a direct relationship between neonatal and maternal factor VIII:C ($r = 0.69$, $P < 0.05$). This disagrees with an earlier study in which factor VIII:C levels in cord blood were found to be unrelated to those in maternal blood at parturition.[8] Conversely, and in confirmation of other reports,[7,10] we found the levels of ristocetin cofactor higher in neonates than in the nonpregnant adults. This parallels the recent finding in fetal but not adult plasma of unusually large von Willebrand factor multimers.[30]

As in other studies[7,9] that assessed both factor VIII:C and vWFAg simultaneously, we found a marked increase in the vWFAg to factor VIII:C ratio in neonates (1.57) that was not significantly different from that observed in mothers (1.56); both values were higher than control values. Such a raised ratio is an objective marker of disseminated intravascular coagulation in extremely ill newborns, especially premature infants.[2,9] The presence of an elevated vWFAg/factor VIII:C ratio in the healthy symptom-free neonate at the time of childbirth may similarly indicate a mild consumptive coagulopathy in cord blood at the time of delivery.[9] Since umbilical venous blood comes in contact with the thromboplastin-rich placenta, it may exhibit a state of activated coagulation. The elevated factor VIII:C and vWFAg levels in maternal blood at the time of childbirth have been ascribed to the extreme stress of labor,[9,10] since these levels decrease to normal adult values in the first three days after delivery.[12,28]

This study, which employed chromogenic microanalytic techniques, has confirmed previous reports of a significant reduction (35-45%) in the levels of antithrombin III, plasminogen,[2,4,7,15,31] and protein C[7,13] in neonates compared with adults; no such differences were noted in the levels of alpha2-antiplasmin. Recent evidence has also shown that fetal and adult antithrombin possess the same molecular weight, charge, and electrophoretic migration pattern,[16,30] and therefore newborns display a quantitative and not qualitative deficiency of antithrombin.

The low neonatal levels of the hemostatic inhibitors, antithrombin III, and protein C, but not alpha2-antiplasmin, are in the range defined for thromboembolic disorders.[32,33] Nonetheless these reduced levels of inhibitors do not represent a significant risk factor of thromboembolism in the healthy newborn. However, in sick neonates, especially those with severe respiratory disease or disseminated intravascular coagulation, antithrombin III levels were shown to drop precipitously below normal adult levels.[2,11,34,35]

The relative deficiency in the various components of the hemostatic mechanism, established in this and many other studies, occurs in otherwise healthy symptom-free neonates. Therefore these alterations should be considered physiological or normal[5] since normal full and preterm infants display adequate hemostasis. Indeed, none of the 300 neonates in our study had any clinical evidence of defective hemostasis.

The reference values obtained in our study are not significantly different from those reported in Caucasian populations (Table 2), and will be used in interpreting hospital laboratory results and in monitoring the effect of therapeutic interventions in various hemorrhagic and thrombotic disorders of the neonate.

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TYPE INCIDENCE OF HERPES SIMPLEX VIRUS IN CLINICAL ISOLATES FROM PATIENTS WITH HERPES GENITALIS

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شملت هذه الدراسة عيِّنات معزولة من ٢٢٨ مريضًا شخصت حالاتهم سريريًا بالحلأ البسيط كانت اثنتان وتسعون منها من مرضى في الهجمة الأولى ومائة وست وثلاثون عينة أخرى من مصابين بحلأ تناسلي راجع. صنفت جميع العينـات بواسـطة مقـايسة الامتصاص المناعي المرتبط بالانظيم، وتبين أن ٥٢ (٥٦,٥٪) من معزولات المجموعة الأولى هي من النمط الأول من حمة الحلأ البسيط (HSV-1) و٤٠ (٤٣,٥٪) من النمط الثاني (HSV-2). أما بالنسبة للمجموعة الثانية فقد عزلت حمة النمط الأول من ١٠ مرضى (٧ر٣٪) وحمة النمط الثاني من ١٢١ مريضًا (٨٩٪) وكلا النمطين معا من خمسة مرضى (٣,٧٪).

يوجد فرق مهم في نسبة وقوع النمط الأول بين خمج الحلأ الأولي والراجع (P < 0.0001)، وربما كان ارتفاع نسبة وقوع النمط الأول في الهجمة الإبتدائية ناتجًا عن التلامس الفمي التناسلي. وقد يكون للنتائج المذكورة أعلاه مغزى فيما يتعلق بتطوير عقاقير ولقاحات للوقاية من الحلأ التناسلي. وقد يثبت أيضًا أن للنمط الأول من حمة الحلأ البسيط دور في تكوُّن ورم عنق الرحم.

Isolates from a total of 228 patients with clinical herpes simplex were included in this study: 92 were from patients in their first episode and 136 were from patients with recurrent genital herpes. All isolates were typed by enzyme-linked immunosorbent assay. In the first episode group, 52 (56.5%) of the isolates were shown to be herpes simplex virus type 1 (HSV-1) and 40 (43.5%) to be type 2 (HSV-2). In patients with recurrent genital herpes, HSV-1 was isolated from 10 (7.3%), HSV-2 from 121 (89%), and both types from five (3.7%). There is a significant difference in the incidence of HSV-1 between the initial and recurrent herpes infection ($P < 0.0001$). The high incidence of HSV-1 in the initial episode may be due to orogenital contact. The above findings have a possible implication in the development of drugs and vaccines in the prevention of herpes genitalis. HSV-1 may also be shown to play a role in the etiology of cervical neoplasia.

Herpes simplex virus (HSV) infection of the genitalia is a sexually transmitted disease that is increasing in incidence.[1,2] Initial exposure to the virus usually produces acute symptoms and severe discomfort, but the disease may also be asymptomatic. After the first episode of infection, the virus becomes latent in the sensory ganglia and patients remain at risk for recurrent herpes.

Herpesvirus hominis is divided into two types: type 1 (HSV-1) and type 2 (HSV-2), distinguished by serologic, biologic, or antigenic criteria. It is generally accepted that there is a difference in the site of involvement and mode of transmission for the two serotypes.[3-5] HSV-1 produces nongenital infections and HSV-2 has been shown to be the major causative agent in genital and neonatal infections.[4] HSV-2 accounts for 89% of the urogenital infections in females and 97% in males.[6] Other reports, however, have indicated that

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HSV-1 may play a greater part in genital infections than was previously thought. Smith et al[7] found that 22% of the genital isolates from females and 9% from males are HSV-1 in the Edinburgh, Scotland, population. In the U.S., Corey et al[8] isolated HSV-1 from genital lesions in 7% of their patients in the first episode of the disease and in only 2% of those with recurrent genital herpes. Kaufman et al,[9] however, isolated HSV-1 from 13.4% of their patients with recurrent disease.

Thus HSV-1 has accounted for a widely different proportion of isolates from patients with first episodes of genital herpes, averaging 7% in Seattle, Washington, U.S., 30% in Northern Ireland, 43% in Japan, and 63% in Sheffield, England.[2,8,10,11] We report here the incidence of HSV-1 and HSV-2 in patients with first episode and recurrent genital HSV infection in Sheffield, England.

Material and Methods

Tissue Culture

Vero cells (Flow Laboratories, Irvine, Scotland) were grown as monolayers in 199 medium containing 10% (v/v) fetal calf serum. Cells were subcultured at a regular interval of 3 days using a split of 1:4.

Viruses

HSV-1, strain F (obtained from Dr. B. Roizman, Chicago,Illinois, U.S.), and HSV-2, strain 333 (obtained from Dr. F. Rapp, Milton Hershey Medical Center, Hershey, Pennsylvania, U.S.), were propagated at a multiplicity of 0.1 to 1 plaque-forming unit per cell in Vero cells.

Isolation of Viruses from Clinical Specimens

Swabs were used to obtain vesicular fluid or specimens from ulcerated lesions of the genitalia or cervix in women and urethra in men and these specimens were used for virus isolation. Upon receipt in the laboratory, the specimens were placed immediately into 2 ml of transport medium; the specimens were then divided into three aliquots and stored at -80°C until tissue cultures were available.

The viruses were isolated and stocks prepared and titrated as described previously.[11]

Identification of HSV Isolates

Viruses isolated from the clinical specimens were typed using an enzyme-linked immunosorbent assay (ELISA) described by Vestergaard and Jensen.[12] Specific antibodies prepared in rabbit serum against HSV-1 and HSV-2 were diluted in coating buffer and 0.1 ml of the preparation inoculated into wells of microtest plates. The plates were left at room temperature. After incubation, the contents of the wells were decanted and plates washed for 3 minutes with PBS-Tween; this was repeated three times. The 100 μl of reference antigens (HSV-1, strain F; HSV-2, strain 333) or clinical isolates, prepared in a series of two-fold dilution in PBS/1% triton-X-100, were each added to a duplicate row of wells; one row was coated with anti-HSV-1 and the second row with anti-HSV-2 antibodies. The plates were incubated at 4°C overnight. The plates then were washed as described above and 100 μl of rabbit anti-HSV-1 or rabbit anti-HSV-2 antibody conjugated to peroxidase was added to wells coated with type-specific antibody for HSV-1 and HSV-2, respectively. These reagents were diluted 1:200 in PBS-Tween + 1% bovine serum albumin (BSA). The plates were then incubated for 1 hour at 37°C. After washing as described above and once with substrate buffer, 100 μl of substrate was dispensed into each well and plates incubated for 10 to 30 minutes at room temperature. The reaction was then stopped by the addition of 50 μl of 2N H_2SO_4 per well. The results were read in a spectrophotometer at 490 nm.

The typing was checked by ELISA utilizing monoclonal antibody, as described by Nilheden et al.[13] Aliquots (200 ml) of Vero cell suspension were seeded into the wells of a flat-bottomed microplate and incubated overnight at 37°C in a humidified atmosphere. The wells were then emptied and 200 μl of undiluted virus isolate added to each of four wells. The plates were incubated overnight in a carbon dioxide incubator. The infected cells were fixed with 0.2% glutaraldehyde (100 μl) for 1 hour and then washed with three changes of PBS-Tween. One hundred microliters of monoclonal antibodies (B1C1 & C4D5) diluted in PBS-Tween with 1% BSA was then added (two wells for each) and the plates further incubated for 1 hour at 37°C and washed as described above. Then 100 μl of antimouse IgG

TABLE 1. *Incidence of HSV type in genital herpes infection.*

	No. of virus type isolated (%)				
Patient	First episode		Recurrence		
sex	HSV-1	HSV-2	HSV-1	HSV-2	Both
Male	12/30(40)	18/30(60)	3/64(5)	59/64(92)	2/64(3)
Female	40/62(64.5)	22/62(35.5)	7/72(10)	62/72(86)	3/72(4)
Total	52/92(56.5)	40/92(43.5)	10/136(7.3)	121/136(89)	5/136(3.7)

TABLE 2. *Incidence of HSV type in relation to infection type.*

Virus type	True primary (%)	Nonprimary first episode (%)	Recurrence (%)
HSV-1	45/75(60)	7/17(41)	10/131(7.6)
HSV-2	30/75(40)	10/17(59)	121/131(92.4)

conjugated to peroxidase was added to each well at a dilution of 1:200. One hundred microliters of substrate was finally added to the wells and plates and incubated for 10 minutes. Results could be read visually or by using a spectrophotometer at 490 nm. Four wells on each plate were used as controls, and HSV-1 and HSV-2 were used as reference antigens in these controls.

Patients

The clinical specimens were obtained from patients with either their first episode of HSV genital infection or a recurrent infection. Swabs were used to take material from external lesions, the endocervix of women, and the urethra of men. First episodes of genital HSV were classified into two groups: (1) true primary infection, occurring in a patient who has had no previous HSV infection as evidenced by lack of serum antibody to both virus types, and (2) nonprimary first episodes in which the first symptomatic genital infection occurs in a patient who already has HSV antibody.[8]

Specimens were collected from 92 patients in the first episode of genital HSV infection. Of these, 62 were female and 30 were male. The mean age was 22.6 (range, 18 to 38) years. Of 92 patients, 75 (82%) had true primary infection. For patients with recurrent infection, HSV was isolated from 136 patients with a mean age of 28.8 (range, 18 to 50) years; 64 were male and 72 were female.

Results

A total of 92 HSV clinical isolates obtained from male and female patients in their first episode of genital HSV infection were typed. The results are shown in Table 1. Fifty-two (56.5%) of the isolates were HSV-1, as typed by ELISA. HSV-1 was more common in females (64.5%) than in males (40%) but was the reverse for HSV-2.

A total of 136 isolates were typed in the patients with recurrent HSV infection. Ten (7.3%) of the isolates were HSV-1. Both HSV-1 and HSV-2 were isolated from five (3.7%) patients (Table 1). Most of the isolates from both men and women with recurrent genital HSV infection were type 2, thus the incidence of HSV-1 in the first episode (56.5%) was significantly less ($P < 0.0001$) than that in recurrent infection (7.3%).

The findings were analyzed according to true primary and nonprimary first episodes, and the results are shown in Table 2. Patients with true primary infections mostly had type 1 virus. In nonprimary and recurrent genital HSV infections most of the isolates were HSV-2. Each type showed an opposite incidence trend (Table 2). No apparent correlation was shown between the causative virus type and the nature of the genital lesion, but there was a significant correlation between the virus type and frequency of recurrence.

Discussion

Genital HSV infection is an important sexually transmitted disease that has increased in incidence in recent years. Reports of patients with genital herpes have suggested that it is not only the cause of physical disability but also produces psychological consequences that can be even more distressing and serious.[14] There is also a close association between HSV infections and cervical neoplasia.[15] The results of the present study and those of Corey et al[8] do not confirm the association of genital herpes with the HSV-2 serotype. HSV-1 was isolated more frequently in our patient population than has been reported from other places.[2,6-10]

In the present study, 56.5% of the isolates from patients (both males and females) in their first episode were HSV-1 and 43.5% contained HSV-2. This confirms the findings reported in a a small group of patients from Sheffield, England.[11] However, we found HSV-2 was more frequently isolated from cases of recurrent genital HSV infection than first episodes, so there is need for differentiating the incidence of HSV-1 according to the clinical manifestation (i.e., true primary, nonprimary first episode, and recurrent infection), as shown in Table 2. HSV-1 was isolated from 60% of the patients with true primary disease compared to 41% of the patients with nonprimary first episode. The reduced incidence of HSV-1 in patients with nonprimary first episode suggests that previous oral HSV-1 infection protects against the acquisition of genital HSV-1 infection.[8]

It is unknown whether prior HSV-1 infection also protects against genital HSV-2 infection. Thus it is concluded that there is a significant difference ($X^2 = 64.53$; $P < 0.0001$) in the type incidence of HSV between the initial and recurrent infection.

The differences in incidence of HSV-1 and HSV-2 between initial and recurrent infections may be due to the lower rate of recurrence of genital type 1 infection compared to genital type 2 infection.[16] The difference in the recurrence rate between types 1 and 2 could be explained by the decreased latency of HSV-1 in the sacral root ganglia compared to HSV-2. This difference between the two virus types may stem from the immunosuppressive ability of HSV-2 that was recently reported.[5]

The increased incidence of HSV-1 in patients in the first episode of infection is due to more frequent oral-genital contact.[8,11] The incidence of HSV-1 in our study is higher than that reported for Northern Ireland. In the present study, 40% of the men and 64.5% of the women with initial infection had HSV-1 whereas in the study from Northern Ireland 60% of the men and 35.5% of the women had HSV-2 infection. In contrast, HSV-1 was isolated from 23.5% of men with genital herpes and 41.3% of women in a study from Northern Ireland conducted during 1982 to 1984. In a study from Edinburgh, Scotland, carried out during 1977 to 1979 these figures were 16% for men and 32% for women. The incidence of HSV-1 for the first episode was higher in females than in males and this may be due to the fact that oral-genital sex is practiced more by females than by males, or it may be due to anatomic variations that may increase the exposure area. Thus the typing of the causative virus is of prognostic importance, and this confirms the conclusions of other reports.[10,11]

Our data agree with that from the Sheffield population[11] concerning the HSV-1 incidence in the first episode, but is in conflict with their finding of an increased incidence in HSV-1 in cases of recurrent infection as well.

The high rate of HSV-1 isolation in the present study has also been reported recently in another study.[2] As mentioned previously, HSV-2 has been shown to be associated with cervical neoplasia,[18,19] and in a recent report, four of five patients with cervical atypia had herpes genitalis caused by HSV-1, which suggests that HSV-1 may play a role in the etiology of cervical neoplasia—perhaps as an initiator.[20] It is also important to take this finding into account when an HSV vaccine is produced for the prevention and control of herpes genitalis. Herpes simplex serotypes show different sensitivities to antiviral agents. It is therefore important to refer to the virus type of a strain tested for drug sensitivity.

Finally, 18% of the patients with initial genital HSV infection had serologic evidence of previous HSV infection, and 82% had true primary infection. This percentage of true primary infection is higher than that reported from Seattle, Washington, in the United States.[8] The higher proportion of patients with true primary genital herpes reflects the particular interest and vigilance in the diagnosis of this form of disease in the United Kingdom.

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BLADDER CANCER IN IRAQ: THE HISTOLOGICAL SUBTYPES AND THEIR RELATIONSHIP TO SCHISTOSOMIASIS

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قيمت ١٢١٦ حالة سرطان مثانة في العراق للتعرف على النمط النسيجي وعلاقته بداء المنشقات. بلغت نسبة الكشف عن بيوض المنشقات حوالي ٣٠٪ فقط. شكلت سرطانات الخلايا الوسفية نصف هذه الحالات تقريبًا وكان معدل تواتر داء المنشقات بينها مرتفعا. بينما شكلت سرطانات الخلايا المتحولة غالبية النصف الآخر من هذه الحالات وكانت مصحوبة بنسبة انتشار منخفضة لداء المنشقات. صاحب داء المنشقات نسبة ٤ر٧٪ فقط من الأورام ذات النمط الحليمي، وهو مايوازي نسبة انتشاره لدى سلاسل الجثث التي قمنا بتشريحها، ولدى جمهور العراقيين البالغين إجمالاً. شوهد كامل الطيف النسيجي من الحؤول إلى الثدن فالسرطان الموضعي في الخزعات المثانية للمرضى المصابين بداء المنشقات، حتى في غياب الغزو السرطاني. أضفنا في دراستنا هذه، وللمرة الأولى على الأرجح في تاريخ الدراسات العراقية، ٨٧ حالة أخذت نماذج الخزاعات منها أثناء قطع المثانة. بينما أخذت الخزعات من الحالات الأخرى أثناء تنظير المثانة عبر الاحليل. وقد ساعد التميحص النسيجي الباثولوجي الدقيق لهذه الحالات على إيضاح العديد من الاستفسارات حول العلاقة بين سرطان المثانة وداء المنشقات لدى العراقيين.

A total of 1216 cases of urinary bladder cancer in Iraq were evaluated for histological type and association with schistosomiasis. The detection rate of schistosomal ova was only about 30%. About half of the cases were squamous cell carcinomas and there was a high frequency of schistosomiasis. The other half of the cases were mostly transitional cell carcinomas, and these were associated with a low incidence of *Schistosoma*. Only 4.7% of the papillary type were associated with schistosomiasis, and this parallels the incidence of schistosomiasis in our autopsy series and in the adult Iraqi population as a whole. The spectrum of metaplasia-dysplasia-carcinoma in situ was observed in the urinary bladder biopsies from patients with schistosomiasis, even in the absence of invasive cancer. In our study, and for most likely the first time in an Iraqi series, we included 87 cases in which biopsy specimens were obtained at cystectomy. In the remaining cases, specimens were obtained during transurethral cystoscopy. Careful histopathological study of these cases helped to clarify many of the questions about the relationship between urinary bladder cancer and schistosomiasis in the Iraqi population.

Carcinoma of the urinary bladder is one of the most prevalent cancers in Iraq. It constitutes about 10% of all malignancies, with a frequency of 11 to 13% in males and 5 to 7% in females.[1,2] These figures are close to those reported in Egypt,[3,4] but there is a much lower incidence of associated schistosomiasis in the Iraqi population (7-29%)[1,5-7] compared to that in Egypt (82-90%).[3,8,9] Even in southern Iraq where schistosomiasis is endemic, Al-Adnani and Saleh[10] reported only a 27.3% association. This led us to speculate that other nonschistosomal factors might be responsible for the high incidence of squamous cell carcinoma in southern Iraq and therefore the relationship of urinary bladder cancer to schistosomiasis in Iraq, whether coincidental or causal, needed to be elucidated. This relationship seems to be well accepted in Egypt but has been questioned in other parts of Africa[11-13] and even in Saudi Arabia.[14]

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Iraq is one of the few countries where the infection is due to the urinary species, *Schistosoma haematobium*, and there is no coexisting *Schistosoma mansoni*. This study was undertaken to evaluate the host response and mucosal changes in the urinary bladder, the histological types of urinary bladder cancer, and the frequency of schistosomiasis for each type.

Material and Methods

A total of 1216 cases of urinary bladder cancer diagnosed at the Medical City Hospital in Baghdad during a 14-year period (1971-1984) were analyzed. Histological sections were reexamined and the tumor types determined using the international histological classification of tumors.[15] Eighty-seven specimens were obtained from partial or total cystectomy, while the remaining 1129 cases were transurethral cystoscopic biopsies. Many blocks (average, ten) were taken in search for schistosomal ova. Schistosomiasis diagnosis was based on the unequivocal identification of ova in tissue sections.

The records of 410 adult autopsies done in our hospital during the same period were reviewed to determine the incidence of schistosomiasis in the autopsy material. In addition, we examined the biopsy records of 188 noncancerous bladder specimens, for the same period, that showed evidence of schistosomiasis to determine the nature of urothelial changes in patients with chronic vesical schistosomiasis.

Histological sections were stained with hematoxylin-eosin. Special stains, including periodic acid-Schiff, alcian blue, and Masson's trichrome, were done in selected cases. Values were statistically analyzed using the chi-square test.

Results

Of the 1216 cases of urinary bladder cancer analyzed, 905 were in males and 311 were in females (2.9:1). Schistosomal ova were demonstrated in the tissue sections of 351 cases (28.9%). Table 1 presents the histological types, their association with schistosomiasis, and the sex ratio. Squamous cell carcinoma formed 46% of the total, and schistosomal ova were detected in 44.8% of these. Transitional cell carcinoma constituted 43.2% of the total, and only 12% of them exhibited schistosomal ova. The lowest frequency of schistosomal ova was in the papillary type (4.7%).

TABLE 1. *Histological types, association with schistosomiasis, and male/female ratio in 1216 cases* of urinary bladder cancer.*

Histological type	No. of cases	Associated schistosomal ova—No.(%)	Male/female ratio
Transitional cell carcinoma	527(43.3)	62(11.8)	4.4/1
Papillary	344(28.3)	16(4.7)	5.5/1
Nonpapillary	183(15.0)	46(25.1)	3.1/1
Squamous cell carcinoma	560(46.0)	251(44.8)	2.0/1
Adenocarcinoma	60(4.9)	22(36.7)	3.0/1
Undifferentiated	56(4.6)	13(23.0)	2.7/1
Others	13(1.0)	3(23.0)	2.3/1
Total	1216	351(28.9)	2.9/1

*Including 87 cystectomies.

TABLE 2. *Association of various histological types of urinary bladder cancer with schistosomiasis in 87 partial and total cystectomy specimens.*

Histological type	No. of cases (%)	Association with schistosomiasis—No. (%)
Transitional cell cancer	43(49.4)	7(16.3)
Papillary	23(26.4)	2(8.7)
Nonpapillary	20(23.0)	5(25.0)
Squamous cell cancer	37(42.5)	29(78.4)
Adenocarcinoma	6(6.9)	3(50.0)
Undifferentiated	1(1.1)	0
Total	87(100)	39(44.8)

The association with schistosomiasis could be better appreciated in the 87 specimens obtained at cystectomy than in those obtained transurethrally. Squamous cell carcinoma formed 42.5% of these cases and 78% were associated with schistosomiasis. While transitional cell carcinoma constituted 49% of the cystectomy cases, only 16% of these cases were associated with schistosomiasis. The association was even less in the papillary type (8.7%) (Table 2). The overall incidence of schistosomiasis for all adult autopsy material at our institution was only 4.4%. This is very close to the 4.9% incidence found in the adult Iraqi popula-

TABLE 3. *Main mucosal lesions seen in 188 cases of noncancerous bilharzial urinary bladders.*

Type of lesion	No. (%)
Von Brunn's nests	26(13.8)
Cystitis cystica and glandularis	35(18.6)
Columnar metaplasia	13(6.9)
Squamous metaplasia	51(27.1)
Basal cell hyperplasia	18(9.6)
Dysplasia	40(21.3)
Carcinoma in situ	5(2.7)
Total	188

tion in 1980, as reported by the Institute of Endemic Diseases in Iraq.[16]

Review of the secondary urothelial changes in cases of noncancerous chronic schistosomal cystitis revealed a wide spectrum of proliferative, hyperplastic, metaplastic, and dysplastic changes (Table 3).

Discussion

In this study we examined closely the possible link between *Schistosoma* and urinary bladder cancer. We have confirmed the previously observed[5-7] low relative frequency of schistosomiasis in Iraqi patients with urinary bladder cancer. The 28.9% incidence observed in our patients is higher than the 4.4% incidence determined from all adult autopsy material at our institution and the 4.9% incidence found in the adult Iraqi population. However, it is much lower than the 82 to 90% incidence reported from Egypt.[3,8,9]

Most of the Egyptian data are drawn from cystectomy specimens, while most of our data were based on findings from small cystoscopy biopsies. It has been argued that some schistosomal lesions may not be sampled during cystoscopy.[1] Our study included 87 specimens obtained during partial and total cystectomies (Table 2). In these cases the percentage of ova-positive malignancies was 44.8%, which is higher than the 28.9% observed in the whole series ($P < 0.001$). We do not believe this difference is due to the effect of selection, because the breakdown by histological type was comparable to that for the series as a whole. However, when the histological types are considered separately, this difference can be attributed to the increase in the association between schistosomiasis and squamous cell carcinoma: 45% in cystoscopy specimens and 78% in cystectomy specimens. This high association is similar to the high incidence reported from Egypt,[8,9,17,18] and is further proof that at least the cases of squamous cell carcinoma, which account for about 50% of all cases of urinary bladder cancer in Iraq, can be considered schistosomal in origin.

The 11.8% association of transitional cell carcinoma with schistosomiasis in Iraq is much lower than that for squamous cell carcinoma ($P < 0.001$). The frequency of schistosomiasis in the papillary form was 4.7% and this rose only to 8.7% for the cystectomy specimens (Table 2). Thus, considering the 4.9% overall incidence of schistosomiasis in the adult Iraqi population as a whole, we conclude that papillary transitional cell carcinoma, which constitutes about 30% of all cases of urinary bladder cancer in Iraq, is essentially nonschistosomal in origin. On the other hand, nonpapillary transitional cell carcinoma represents a heterogeneous group, both schistosomal and nonschistosomal. The incidence of schistosomal ova was about 25%, half the incidence seen in squamous cell carcinoma ($P < 0.001$) and about five times that seen with papillary transitional cell carcinoma ($P < 0.001$). These conclusions agree with the preliminary results from an ongoing study of risk factors in urinary bladder cancer being conducted at our institution.[19] Of the 135 patients studied so far, 41% had squamous cell carcinoma, and of these, 82% had a clinical or histological diagnosis of schistosomiasis. Ninety-two percent of the patients with squamous cell carcinoma came from endemic areas and 55% of them had agrarian lifestyles. Of the 50 patients with papillary transitional cell carcinoma, 30% of the cases were associated with schistosomiasis; 44% of the patients came from endemic areas and 26% of them were peasants.

Adenocarcinoma is not uncommon in Iraq (approximately 5%) and many cases are associated with schistosomiasis (approximately 37%). They are frequently metaplastic, with squamoid areas or even mixed adenosquamous carcinomas. We believe that schistosomal cancers arise in a metaplastic epithelium and can become either adenomatous or squamous, but usually the latter. For the first time in a series from Iraq, we reviewed the secondary urothelial changes in chronic vesical schistosomiasis in 188 patients (Table 3), and discovered a wide spectrum of proliferative, metaplastic, and dysplastic changes. Such changes are also seen in patients with urinary bladder cancer and schistosomiasis. Our findings parallel those of Khafagy et al[20] in Egypt. Thus a similar metaplasia-dysplasia-carcinoma sequence can be postulated in chronic vesical schistosomiasis in Iraq.

The nonschistosomal cancers were predominantly transitional, while squamous cancers constituted only 16.7% of the cystectomy series. This figure is very close to the incidence of squamous cell carcinoma in some countries where schistosomiasis is not endemic.[21] On the other hand, these findings contrast sharply with the Egyptian experience,[8] where even in nonschistosomal cancers, squamous cell carcinoma predominates (50%). Thus factors other than schistosomiasis, which is postulated to contribute to the high incidence of squamous cell carcinoma in Egypt[8] and Uganda,[11] are not operant in Iraq.

Ultimately we believe that the current campaign against schistosomiasis will reduce the incidence of schistosomal cancer in Iraq within the next two decades or so.

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ROLE OF PLASMIDS IN THE ANTIBIOTIC RESISTANCE OF BACTERIA IN ASIR PROVINCE

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حللت مائة وخمسة معزولات جرثومية سريرية ذات أنماط متباينة من الاستجابة للصادات بحثًا عن وجود دنا البلازميد. وجدت أعلى نسبة مئوية من دنا البلازميد في معزولات الاشريكية القولونية (٥٥٪) ومعزولات الكلبسيلة الرئوية (٥٠٪) ومعزولات الزائفة الزنجارية (١٢,٥٪). ولم يكن هناك ترابط مطرد بين عدد أنواع البلازميدات في الخلية الواحدة وبين أنماط المقاومة للصادات ولكن وجد ترابط بين البلازميدات المعزولة والأنماط الظاهرية للمقاومة. ويناقش هذا المقال مغزى غياب دنا البلازميد من المعزولات المقاومة للصادات وما يثيره هذا الغياب من قلق. كما يناقش أيضًا إمكانية استخدام هذا الأسلوب لتقفي تنقل الأخماج.

One hundred and five clinical isolates with different antibiotic susceptibility patterns were analyzed for the presence of plasmid DNA. The highest percentages of plasmid DNA were found in *Escherichia coli* isolates (55%), *Klebsiella pneumoniae* isolates (50%), and *Pseudomonas aeruginosa* isolates (12.5%). The number of plasmid species per cell did not always correlate with the antibiotic resistance patterns; however, the plasmids isolated were found to correlate with the resistance phenotypes. The significance of and resulting concern stemming from the absence of plasmid DNA in the antibiotic resistance isolates are discussed. The potential use of this approach for tracing cross infections is also discussed.

The increased use of antibiotics for disease treatment and prevention, for promotion of growth in animals to increase protein yield, and for plant protection has been accompanied by the increasing appearance of antibiotic-resistant strains of bacteria.[1-3] The problems resulting from this are being felt worldwide, and in Saudi Arabia, numerous reports and conferences have documented and assessed the emergence of such resistant strains.[4-18]

Bacteria resist antibiotics either by modifying the intracellular targets or by preventing the antibiotics from reaching their targets.[3,19-22] The latter mechanism involves either inactivation of the antibiotic by bacterial coded enzymes or alteration of the cell's permeability, thus blocking entrance of the antibiotic. Additionally, bacteria may be intrinsically resistant to antibiotics through as yet unexplained or identified mechanisms. The principal concern of microbiologists is drug resistance stemming from the transfer of resistance determinants to sensitive strains. Numerous experiments have demonstrated that bacteria can transfer genes capable of expressing resistance, both within species and between genera.[3,20] The transferred genes, often as plasmids, may become integrated into the bacterial chromosome, thus giving permanence and phenotypic expression to the resistant determinants.

We describe the results of a study that was designed to: (1) show the magnitude of antibiotic resistance in selected bacteria isolated from patients admitted to a hospital in the Asir region of Saudi Arabia; (2) screen these strains for plasmid-borne antibiotic resistance; and (3) test the feasibility of using the plasmid profile analysis to show strain relationships and demonstrate the potential of the technique in tracing cross infections.

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Material and Methods

All strains were isolated over a six-month period from various clinical material submitted to the clinical microbiology laboratory of an acute care hospital located in the Asir region of Saudi Arabia. The API 20 "enteric" and API 20 "nonenteric" systems (API System; S. A. Montalieu Vercieu, France) were used to identify strains of Enterobacteriaceae and Pseudomonadaceae, respectively.

The in vitro response of the strains to seven antibiotics was determined by the single-disk agar diffusion method of Bauer et al.[23] The seven antibiotics used in the present study were selected according to the following criteria: (1) the availability of the agents; (2) the extensive use of the agents in treating infections; and (3) the prescribing patterns of the physicians in the hospital. The standard antibiotic-impregnated disks were manufactured by Baltimore Biological Laboratories (a subsidiary of Becton Dickinson and Co., Cockeysville, MD) and contained: amikacin, 10 μg; ampicillin, 10 μg; cephalothin, 30 μg; chloramphenicol, 30 μg; gentamicin, 10 μg; tetracycline, 30 μg; and tobramycin, 10 μg. American-type culture collection strains (ATCC) *Escherichia coli* 25922 and *Pseudomonas aeruginosa* 27853 were used as controls in all antibiotic sensitivity tests. These two strains have been designated by the National Committee for Clinical Laboratory Standards (U.S.A.) for monitoring the accuracy and precision of the disk diffusion tests when assessing any gram-negative Enterobacteriaceae or Pseudomonadaceae bacillus.

Single clones were picked from agar plates and inoculated into 3-ml LB (Luria-Bertani) broth, with or without 50 μg/ml of ampicillin. Cultures were grown overnight at 37°C with aeration in a shaker incubator. Aliquots (0.5 ml each) of the cell suspensions were mixed with glycerol to a final concentration of 20% and kept frozen at –70°C. The remaining 1.5 ml of each culture was centrifuged for 1 minute in an Eppendorf centrifuge. The cell pellets were either used immediately for isolation of plasmid DNA or kept frozen at -70°C.

Plasmid DNA was isolated from bacterial cell pellets by the alkaline lysis method of Birnboim and Doly,[24] as modified by Ish-Horowicz.[25] The dried plasmid DNA samples were dissolved in 30 μl of 10 mM TRIS-Cl + 1 mM EDTA (TE buffer, pH 8).

Plasmid DNA samples were analyzed by electrophoresis on 1% agarose gels (20 × 20 cm) at 50 V for 12 hours using TRIS-borate (pH 8). After the electrophoretic run, the gels were stained with ethidium bromide (0.5 μg/ml) and photographed using Kodak Tri-X pan films (ISO 400/27; No. 191 2104).

The isolated plasmid DNA from each isolate was used for transforming *E. coli* HB101 according to the method described by Hanahan.[26] The transformed *E. coli* was spread on LB agar plates and the antibiotic susceptibility tested by the method of Bauer et al.[23]

Results

The results of testing the susceptibility of selected bacteria isolated from patients admitted to the Asir hospital are summarized in Table 1. Both *E. coli* and *K. pneumoniae* showed a significant resistance to ampicillin (69% and 97%, respectively) and to tetracycline (83% and 97%, respectively). The 100 *P. aeruginosa* strains showed 100% resistance to all agents tested other than the aminoglycosides. Although the organism

Table 1. *Antibiotic resistance of selected gram-negative bacilli of the Asir facility.*

	Antibiotic tested (% resistance)						
Organism (100 isolates)	AMK	AMP	C	CF	GN	TE	TOB
Escherichia coli	*	60	9	9	3	83	*
Klebsiella pneumoniae	*	97	23	13	27	97	*
Pseudomonas aeruginosa	3	100	100	100	16	100	3

* = not tested routinely; AMK = amikacin; AMP = ampicillin; C = chloramphenicol, CF = cephalothin, GN = gentamicin, TE = tetracycline, TOB = tobramycin.

shows only slight resistance to amikacin and tobramycin (3%), 16% of the *Pseudomonas* isolates are resistant to gentamicin.

The results of screening for plasmid DNA are shown in Figures 1 to 4. Electrophoretic analysis of 20 *E. coli* isolates revealed multiple antibiotic resistance patterns (Figure 1) with the exception of one isolate (lane 9 in Figure 1), which was resistant only to tetracycline. Eleven *E. coli* isolates carried plasmids. Five (lanes 1 to 5) had multiple plasmid patterns and six (lanes 6 to 11) had single plasmids. The plasmids in the five isolates in lanes 1 to 5 are compatible, since the repeated streaking (15 times) of single clones on agar plates, and subsequent analysis of several single clones from each new plate, showed persistence of the original multiple plasmid patterns. The relative sizes of the different plasmids are compared to the size of superhelical pBR 322 (4362 b.p.) in lane 12 of Figure 1, which migrates faster than the 4.4-kB restriction fragment of the lambda *Hind* III digest (used as a marker) in lane 13.

Figure 2 shows the results of analyzing 26 *K. pneumoniae* isolates with either ampicillin resistance only (isolates 2, 4, 10, 11, 12, and 13) or multiple resistance patterns (isolates 1, 3, 5, 6, 7, 8, and 9). As shown in Figure 2, 13 of 26 isolates had plasmid patterns. Isolates 1 and 2 had a single plasmid, while isolates 3 to 12 had multiple plasmid patterns. Isolate 9, which is resistant to ampicillin, contains a doublet (see lane 9 in Figure 2).

Only five of 40 *P. aeruginosa* isolates contained plasmids, as shown in Figure 3. Although the five isolates had multiple antibiotic resistance patterns, only isolate 1 showed a multiple plasmid pattern (lane 1 in Figure 3).

Several other members of the Enterobacteriaceae family, isolated in small numbers, were analyzed for the presence of plasmids. As shown in Figure 4, one strain each of *Enterobacter cloacae* (lane 1), *Serratia marcescens* (lane 2), and *Shigella dysenteriae* and *S. flexneri* (lanes 3 and 4, respectively) showed multiple plasmid patterns. Also, two isolates of *Shigella sonnei* showed multiple plasmid patterns (lanes 5 and 6). Table 2 summarizes the results shown in Figures 1 to 4.

When *E. coli* HB101 was transformed with the isolated plasmids, the antibiotic susceptibilities of the *E. coli* recipients were almost identical to those observed in the original donors. Three *E. coli* and two *P. aeruginosa* isolates, however, lost their resistance to cephalothin.

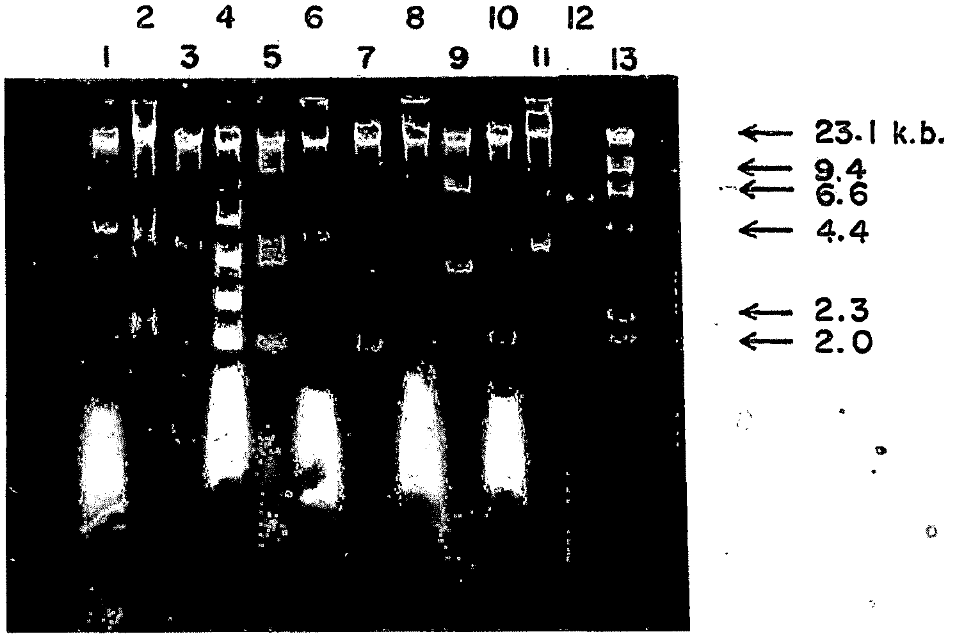

FIGURE 1. Agarose gel electrophoresis of partially purified *Escherichia coli* plasmid DNA. Plasmid DNA from *E. coli* isolates dissolved in 30 μl of TE buffer were applied on a 1% agarose gel (lanes 1-11). Purified pBR 322 and lambda *Hind* III digest were applied on lanes 12 and 13, respectively, as markers for determining the relative plasmid sizes.

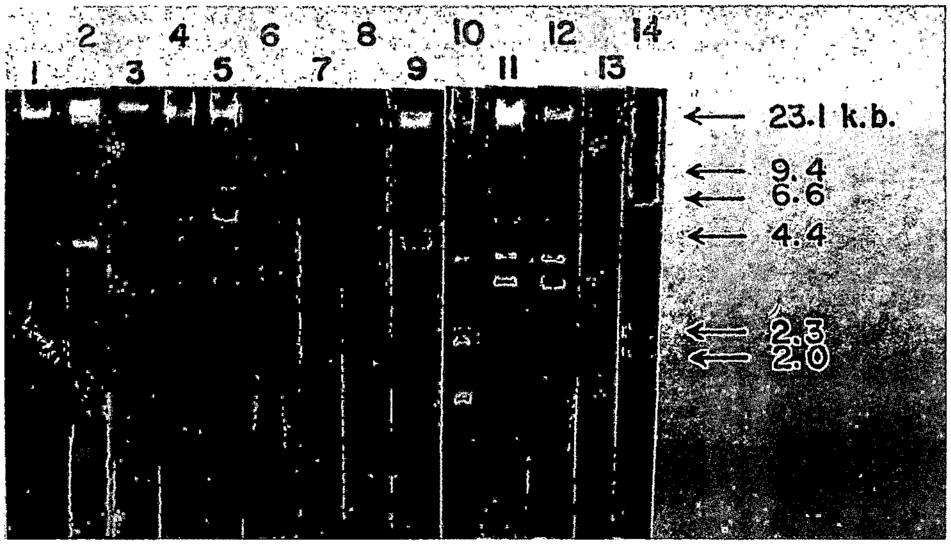

FIGURE 2. Agarose gel electrophoresis of partially purified *Klebsiella pneumoniae* plasmid DNA. Plasmid DNA from *K. pneumoniae* isolates in TE buffer was applied on a 1% agarose gel (lanes 1-13). On lane 14, lambda *Hind* III digest was used as a size marker.

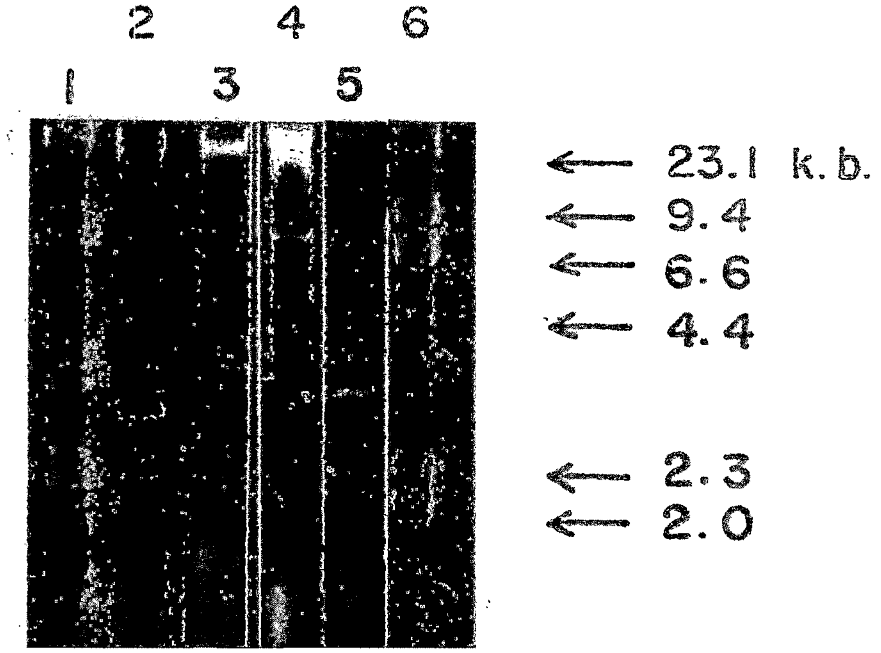

FIGURE 3. Agarose gel electrophoresis of partially purified *Pseudomonas aeruginosa* plasmid DNA. Plasmid DNA from *P. aeruginosa* isolates dissolved in TE buffer was applied on 1% agarose gel (lanes 1-5). Lambda *Hind* III digest was applied on lane 6 as a size marker.

Discussion

The increase in antibiotic-resistant strains of bacteria in Saudi Arabia has been observed for several years. Bacterial resistance patterns to antibiotics differ markedly in different parts of the world. The data shown in Table 1 more or less agree with the patterns from other parts of Saudi Arabia.[4,5,17,18] In the present study, 105 clinical isolates with multiple antibiotic resistance were screened for the presence of plasmids. A total of 35 isolates contained one or more plasmids of

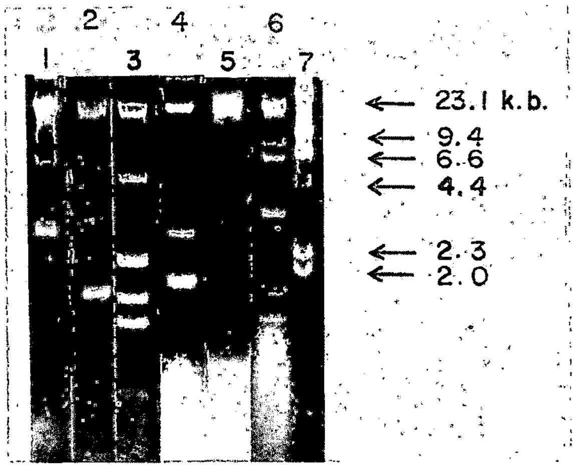

FIGURE 4. Agarose gel electrophoresis of partially purified plasmid DNA from selected members of the Enterobacteriaceae family. Plasmid DNA in TE buffer was applied on 1% agarose gel in the following order: *Enterobacter cloacae* (lane 1), *Serratia marcescens* (lane 2), *Shigella dysenteriae* (lane 3), *Shigella flexneri* (lane 4), and *Shigella sonnei* (lanes 5 and 6). Lambda Hind III digest was applied as a size marker in lane 7.

varying sizes. The presence of plasmid DNA in 33% of the isolates tested is much lower than the figure of 65% reported by Skotnicki et al[28] in a similar study performed at King Faisal Specialist Hospital in Riyadh. This difference may be due to different strains of bacteria tested or to a decreased incidence of plasmid DNA integration into bacterial chromosomes in the Riyadh area. The significant feature in the plasmid patterns of most isolates was the lack of correlation between the number of plasmids present and the phenotypic expression of antibiotic resistance. The absence of plasmid DNA in 70 of the clinical isolates indicates that the determinants of antibiotic resistance are carried on the chromosomes of these strains.[8,27]

The plasmid profiles shown in Figure 1 for *E. coli* isolates indicates the presence of a small plasmid which migrates in a manner similar to the 2 kB *Hind* III fragment of the lambda marker, in the isolates applied to lanes 1, 2, 3, 4, 7, and 10. Also, several other isolates have similarly sized plasmids in common. Detailed characterization of these plasmids, using restriction analysis and blot hybridization, is in progress.

The isolates in lanes 4 and 5 of Figure 2 were collected from two different infants in the same nursery, and thus are related epidemiologically.

TABLE 2. *Summary of isolates analyzed for presence of plasmids.*

Isolate	No. of isolates analyzed	No. of isolates with one plasmid	No. of isolates with more than one plasmid	% of plasmid-positive isolates
E. coli	20	6	5	55
Klebsiella pneumoniae	26	6	11	50
Pseudomonas aeruginosa	40	4	1	12.5
Enterobacter cloacae	1	1	–	–
Serratia marcescens	10	1	–	10
Shigella dysenteriae	1	–	1	–
Shigella flexneri	1	–	1	–
Shigella sonnei	3	–	2	–
Salmonella sp.	1	–	–	–
Salmonella paratyphi A	1	–	–	–
Salmonella enteritidis	1	–	–	–

The first isolate (lane 4) came from the spinal fluid of an infant in whom meningitis developed. Two days later, sepsis developed in a second infant in the same nursery, and *K. pneumoniae* was isolated from her blood (lane 5). This second isolate lacked two plasmids seen in the first isolate shown in lane 4, and also contained a plasmid species that did not exist in the first isolate shown in lane 4. Both isolates, however, had four similarly sized plasmids. The plasmid patterns of these two isolates (lanes 4 and 5) may depict the transfer of the organism from the first to the second infant. The isolates in lanes 11 and 12 of Figure 2 came from the same patient, in specimens obtained on two consecutive days, and showed identical plasmid profiles. The precision and validity of using the plasmid profile as preliminary evidence of strain relatedness were thus demonstrated.

Several other members of the Enterobacteriaceae family were analyzed to document their plasmid patterns for future use in outbreaks of infections in our facility (Figure 4).

From the results of the present study, we have drawn the following conclusions: 1. The plasmid profile (single versus multiple) of the species tested does not necessarily correlate with the antibiotic resistance patterns. 2. The percentages of isolates of certain bacterial species harboring plasmid DNA are low. It is possible that some of the plasmid-negative, resistant isolates may have integrated the resistance determinants into their chromosomes. The release of these resistance genes from the host bacterial chromosomes could facilitate modification of the antibiotic susceptibility characteristics of other strains. 3: Despite the clear-cut results in our study, the lack of similar studies originating from other areas of the Kingdom poses difficulty in assessing the situation for the country as a whole. The only other report[28] from Saudi Arabia showed a higher incidence of plasmid-borne antibiotic resistance in strains from the King Faisal Specialist Hospital in Riyadh. These other results included data from 150 clinical isolates, but there was no defined correlation between plasmid profiles and bacterial species. 4. A more controlled and selective use of antibiotics by clinicians and veterinarians is needed as part of the solution to the problem of antibiotic-resistant bacteria.

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NASOPHARYNGEAL CARCINOMA IN SAUDI ARABIA: SELECTED CLINICAL AND EPIDEMIOLOGICAL ASPECTS

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أجريت دراسة مراجعة لثلاثمائة وواحد وثمانين مريضا بسرطانة البلعوم الأنفي المؤكدة نسيجيا كانوا قد أحيلوا إلى مستشفى الملك فيصل التخصصي ومركز الأبحاث من جميع مناطق المملكة على مدى عشر سنوات ونصف (من حزيران ١٩٧٥م إلى كانون أول ١٩٨٥م)، وأظهرت الدراسة كثرة توارد أورام المرحلة الرابعة (٩٣٪) ووجود نقائل بعيدة لدى ١٧,٣٪ منهم عند التشخيص. كانت نسبة وقوع السرطانة الوسفية المتقرنة منخفضة جدا (٢٪) واعتبر ذلك نتيجة لصغر سن جمهرة المرضى نسبيا. فقد أظهر تحليل الأعمار أن ذروة الوقوع كانت في مجموعة الأعمار من ٤٥ إلى ٥٥ عاما، وكانت هنالك ذروة أصغر في مجموعة الأعمار من ٢٠ إلى ٢٤ عاما لدى كل من الذكور والاناث، علما بأن ذروة الوقوع في الفئة الأصغر سنا قد انخفضت عندما قوبلت أعداد المرضى بالاحصائيات المتوافرة عن التعداد العام للسكان.

A retrospective review of 381 patients with histologically confirmed nasopharyngeal carcinoma referred from all regions of Saudi Arabia to the King Faisal Specialist Hospital and Research Centre during the $10^{1}/_{2}$-year period (June 1975 to December 1985) demonstrated a high frequency of stage IV tumors (93%), with 17.3% having distant metastases at presentation. There was a very low incidence (2%) of keratinizing squamous cell carcinoma, considered due to the relatively young age of the population. Age analysis indicated a peak incidence among the referred cases in the 45-55 age group, with a smaller peak in the 20-24 age group for both males and females, although the younger age peaks were reduced when the patient numbers were standardized for available population census figures.

Nasopharyngeal carcinoma is known to be a relatively rare cancer in most countries, with the highest incidence reported from southern China. Other populations with a high or moderately high incidence are in Malaysia, Indonesia, Singapore, Thailand, and Vietnam. There is also an alleged increased frequency in the Sudan, East Africa, and parts of North Africa adjacent to the Mediterranean.[1,2] The incidence of nasopharyngeal carcinoma cannot be defined in Saudi Arabia at this time, as there is no population-based cancer registry.

In 1974, the King Faisal Specialist Hospital and Research Centre (KFSH) was established in Riyadh as the major referral center for cancer in Saudi Arabia. This institution has its own computerized tumor registry and is currently the best available source of information about nasopharyngeal carcinoma in Saudi Arabia. Patients with histologically confirmed squamous cell carcinoma of primary nasopharyngeal origin referred from all regions of the country were retrospectively analyzed for selected clinical and epidemiological features and form the basis of this report.

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Material and Methods

Between June 1975 and December 1985, a total of 11,107 patients with cancer referred from all regions of Saudi Arabia were entered in the KFSH tumor registry using a PDP-11 computer equipped with Fortran and Datatrieve. Of these, 399 patients had histologically confirmed primary nasopharyngeal carcinoma. Personal, clinical, and radiographic data were obtained from a detailed retrospective review by one of us (B.C.) of the medical record charts and radiographs. Eighteen medical records were inadequate for any aspect of review, leaving 381 patients with evaluable data. Data were then entered and organized on an IBM-PC/XT database package. Subsequent analyses were carried out using the Statgraphics Statistics package on the Tandon PCA-20 microcomputer.

Age distribution of the patients was studied separately for males and females and represented on histograms with five-year intervals, beginning at age zero, as is customary for WHO data. Because of the limited reliability of available population statistics for the years of this study, correction of these age distributions was limited to a change in the shape of these histograms by expressing all relative incidence data as a percentage of the largest incidence within each histogram.

The geographic distribution of referred patients from within Saudi Arabia was done according to eight regions whose boundaries were defined by administrative and topographic features. Again, because of the limitations of census information, any attempt to define the relative geographic distribution of patients was limited to a comparison of the percentage of referred patients to the percentage of total population for each of the defined regions.

Tumors were staged according to the American Joint Committee (AJC) on Cancer Staging and End Results Reporting.[3]

Pathological material that was routinely stained with hematoxylin-eosin was reviewed by one of us (M.A.A.) and histologically classified according to the predominant histological pattern, as proposed by the WHO classification.[4] The only information available to the pathologist was the biopsy site and age and sex of the patient.

Results

Age and Sex Distribution

This study revealed a predominance of male (N = 287) to female (N = 94) patients; ratio, 3:1. Figures 1 and 2 show the age distribution for males and females, respectively. These numbers reflect the actual numbers of patients recorded at KFSH for the defined years of the study. Each of these figures clearly shows evidence of a bimodal distribution with a small peak in the 20-24 age group and a larger peak at 45-55 years. Both peaks occur for the same age groups in both men and women, but the female age distribution differs from the males' in that the actual proportion of females associated with the smaller, younger peak is greater than that for the males. Twenty-seven of 94 (29%) female patients were less than 30 years of age, compared with 94 of 227 (19%) male patients. Thus the two peaks are more distinct for the female group.

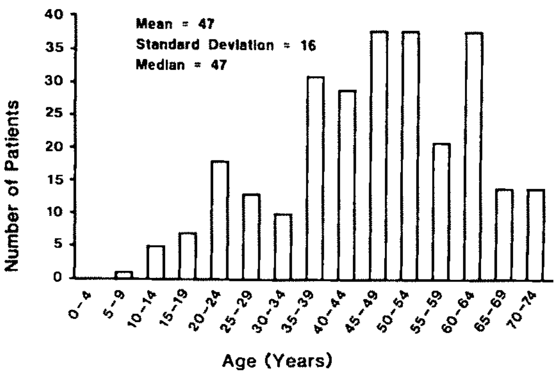

FIGURE 1. Actual number of males with nasopharyngeal carcinoma registered at KFSH between June 1975 and December 1985.

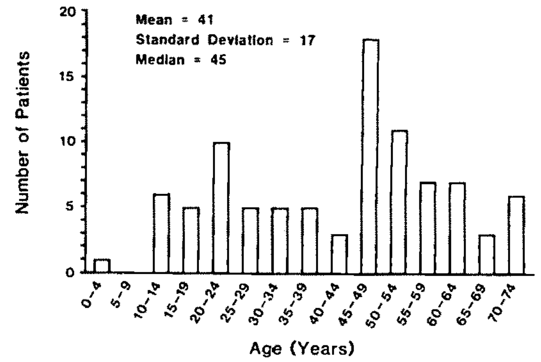

FIGURE 2. Actual number of females with nasopharyngeal carcinoma at KFSH between June 1975 and December 1985.

Figures 3 and 4 show the equivalent male and female data, corrected for the available population statistics, regarding the standardized frequency of the disease expressed as a percentage of the largest group. Evidence of the initial distribution survives in these plots. Although the younger peak is considerably reduced, it is still evident in the 20-24 year age group.

Geographic Distribution

The highest referral rate was 138 patients (36%) from region 1 (Riyadh). Next in order were 71 patients (18%) from region 3 (Medina); 58 patients (15%) from region 2 (Jeddah); 48 patients (12%) from region 4 (Dammam); 33 patients (8%) from region 6 (Gizan); 25 patients (6%) from region 5 (Tabouk); and 9 patients (2%) from region 1a (Qassim). Seventeen patients (4%) were referred from regions outside Saudi Arabia and no patients were referred from region 7 (Rub Al-Khali).

Figure 5 shows the distribution of the referred patients relative to the population, expressed for each region as the ratio of the percentage of referred patients to the percentage of total population. If the patient referral rate and true incidence were evenly distributed throughout the country, then this ratio should be unity for all regions. A ratio greater than unity was noted in region 1 (Riyadh) and region 2 (Jeddah). All other regions exhibited ratios less than unity.

Clinical Presentation

Figures 6 and 7 give the number of patients presenting with a particular symptom or sign, respectively. Most patients presented with multiple clin-

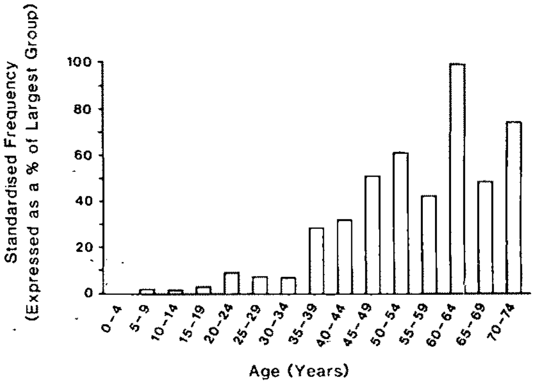

FIGURE 3. The correction of frequency from available population statistics for males. Each group is expressed as a percentage of the largest group.

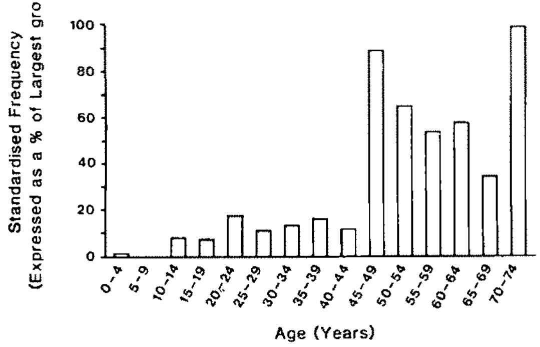

FIGURE 4. The correction of frequency from available population statistics for females. Each group is expressed as a percentage of the largest group.

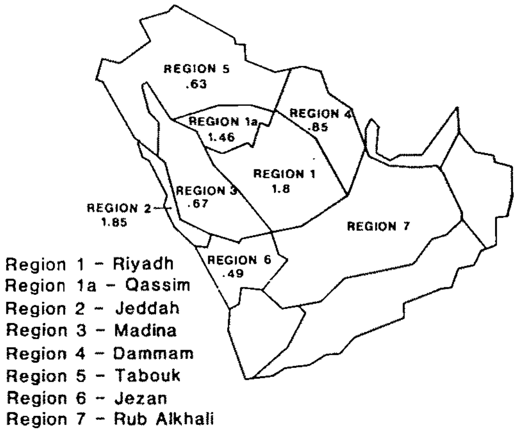

FIGURE 5. Geographic distribution of referred patients with nasopharyngeal carcinoma expressed as a ratio of percentage of referred patients to percentage of total population for seven defined regions.

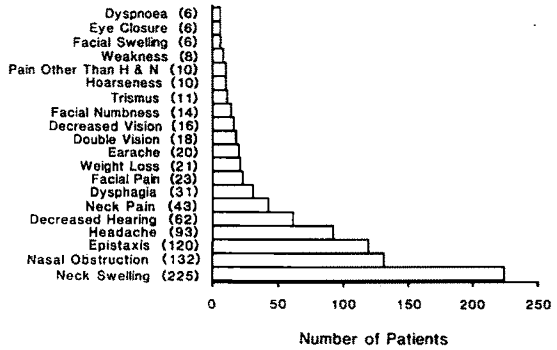

FIGURE 6. Actual number of patients presenting with one or more symptoms.

ical manifestations, although the most frequent was neck swelling. Many of the clinical features reflected advanced stage of disease at presentation. The mean duration from onset of symptoms to diagnosis was nine months.

Staging

The records of 36 patients were insufficiently documented to allow for accurate staging of their tumors based on the AJC Committee recommendations. Of the remaining 345 patients, 286 (83%) had tumors confined to the nasopharynx and regional cervical lymph nodes. Table 1 gives the TN associations for this group and demonstrates the high frequency of stage IV tumors (266 patients; 77%). There were only 20 patients with less advanced tumors (one patient with stage I, two patients with stage II, and 17 patients with stage III). Fifty-nine patients (17%) had distant metastases at presentation and of these the majority, 37 patients, had skeletal metastases. Other sites of metastasis were the liver, eight patients; axilla, five patients, abdomen, five patients; and lung, four patients.

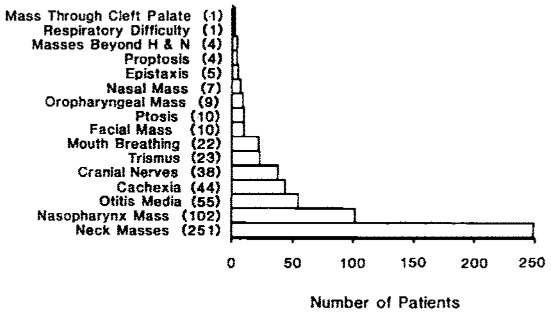

FIGURE 7. Actual number of patients presenting with one or more physical signs.

TABLE 1. *TN groupings of 286 patients with nasopharyngeal carcinoma confined to nasopharyngeal and regional cervical lymph nodes.*

Primary extent	Nodal extent					
	N0	N1	N2A	N2B	N3A	N3B
T0	0	7	0	2	5	6
T1	1	2	5	2	4	12
T2	2	6	5	7	12	33
T3	3	3	1	7	5	34
T4	10	8	5	35	5	59

Pathology

The histopathological review based on light microscopy findings revealed the majority, 289 patients (76%), had nonkeratinizing squamous cell carcinoma, while 84 patients (22%) had undifferentiated carcinoma and only eight patients (2%) had squamous cell carcinoma. Fifteen percent of the patients showed an excess of eosinophils in the stroma. Five percent of the patients showed features of focal anaplasia. Amyloid was seen in 1.5% of the cases.

Discussion

The 399 patients recorded on the KFSH tumor registry between June 1975 and December 1985 with nasopharyngeal cancer constitute 30% of the total number of patients (1,301) with "head and neck" cancer (ICDO categories 140-149, 160-161) and 3.6% of the total cancer population (11,107) patients. The absolute incidence rate of nasopharyngeal carcinoma in Saudi Arabia cannot be calculated based on the observations from the present study because the tumor registry, being hospital-based, is totally dependent on referral patterns. A previous study of 7,251 histologically confirmed new cases of cancer sequentially referred to KFSH for the six-year period 1979-1984 showed nasopharyngeal cancer ranked ninth in crude relative frequency for all patients, and when considered separately, the males ranked sixth and females fourteenth in crude relative frequency.[5]

The age distribution of our patients indicates a major peak in the 45-55 year age group for both males and females. While the existence of a "middle aged" peak is consistent with findings in the literature, the existence and significance of a second peak at an earlier age is more speculative. Second smaller peaks have been reported for patient populations in Bombay, India, 13-22 years;[6] Puerto Rico, 20-24 years;[7] and Tunisia, 10-19 years.[8]

The geographic distribution of referred cases of nasopharyngeal cancer to KFSH should not necessarily be interpreted as an indication of geographic variation in the incidence of the disease. The differences more likely reflect referral bias, and this is supported by the observation that similar ratios occur when considering the geographic distribution for all cancer patients referred to KFSH.

A high percentage of our patients with nasopharyngeal cancer present late, with clinical features consistent with stage IV tumors. This trend is not unique to this type tumor. A previous stage analysis on 1,301 patients with histologically confirmed cancer of the head and neck referred to KFSH during the same time period of this study showed that a majority of patients presented with advanced tumors, with 29.7% having stage III and 58% stage IV disease.[9] The higher percentage of stage IV nasopharyngeal tumors is most likely due to the relatively concealed site of the primary tumor compared to other sites in the head and neck. The tendency for patients with head and neck cancer to present "late" in the disease is related to a number of factors, including a lack of patient awareness of the significance of their symptoms and patient distance from medical facilities.

There is a very low incidence (2%) of keratinizing squamous cell carcinoma in our study. By comparison, keratinizing squamous cell carcinoma constituted a 20% incidence among 363 patients from Singapore, using the same WHO classification.[10] The relative frequency of keratinizing squamous cell carcinoma is known to increase with age. It has been estimated that approximately 60% of people in Saudi Arabia are under the age of 20 years, and this may explain why so few cases of keratinizing squamous cell carcinoma were seen in the study.

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ENDOSCOPIC DILATATION IN THE MANAGEMENT OF BENIGN AND MALIGNANT ESOPHAGEAL STRICTURES: RESULTS OF 203 CONSECUTIVE DILATATIONS

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أجريت عمليات مجموعها (٢٠٣) لتوسيع المريء بالتنظير الباطني على ٨٣ مريضا، ممن يعانون من تضيق حميد أو خبيث وذلك باستعمال موسعات مختلفة. وكان من هؤلاء ست وثلاثون ممن يعانون من تضيق حميد ٢ , ٧٨٪ اختفت أعراض التضيق لديهم بعد عملية توسعة واحدة إلى ثلاث عمليات في خلال فترة متابعة بلغ متوسطها ثمانية أشهر ونصف الشهر. بينما كان سبعة وثلاثون منهم يعانون من تضيق خبيث، تراجع عسر البلع لدى أربعة عشر مريضا منهم عقب التوسعة الأولى فألغى الحاجة إلى ادخال أنابيب التغذية أو أنابيب اتكنسون. أصيب ١٧ مريضا (٥ , ٢٠٪) بعسر البلع عقب عملية جراحية على المريء وتحسنت حالتهم عقب التوسعة بالتنظير الداخلي. فَشِلت عملية التوسعة في أربعة مرضى وحدث انثقاب المريء لدى مريض كان يعاني من تضيق خبيث. لم تحدث أية وفاة بين المرضى الذين أجريت لهم عمليات توسعة بالتنظير الداخلي.

Eighty-three patients with benign or malignant strictures underwent 203 endoscopic esophageal dilatations using different types of dilators. Of these, 36 patients (78.2%) with benign strictures became free of symptoms after one to three dilatations, during a mean follow-up period of 8.5 months. Thirty-seven patients had malignant strictures; in 14 dysphagia abated after the initial dilatations without the need to insert feeding or Atkinson tubes. Seventeen patients (20.5%) had dysphagia following esophageal surgery and their condition improved following endoscopic dilatations. Dilatation failed in four patients and esophageal perforation occurred in one patient with malignant stricture. There was no mortality among our patients that was directly related to endoscopic dilatations.

Esophageal strictures of various etiologies have been managed conservatively, and endoscopic esophageal dilatation is one such measure that has been used for many years to treat esophageal stenosis and dysphagia.[1,2] The use of fiberoptic endoscopes with different dilators has made dilatation simpler and safer and it is being performed more frequently for both benign and malignant esophageal strictures. Different dilators can be used depending on the type of strictures.[3] For mild to moderate strictures, mercury-filled dilators (Maloney) can be used. In more severe cases, a spring-tipped metal guidewire can be passed through the stricture under direct vision, followed by Eder-Puestow or savary dilators; for cases of achalasia, pneumatic or balloon dilatations can be carried out. Endoscopic palliation or insertion of different types of tubes can also be performed. This nonsurgical procedure carries less morbidity and mortality compared to surgery. We report our experience at the Riyadh Armed Forces Hospital, which is a main referral center for different specialties including gastroenterology and oncology.

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Material and Methods

A total of 10,938 upper gastrointestinal tract endoscopic procedures, including esophageal dilatations, were performed at the Gastroenterology Unit, Riyadh Armed Forces Hospital, between June 1982 and December 1988. There were 203 endoscopic esophageal dilatations performed on 83 patients with benign or malignant strictures who were referred because of problems with dysphagia. Stricture in each case was diagnosed by endoscopy (sometimes preceded by radiology). During endoscopy, assessment of the stricture was made, and when indicated, sufficient biopsy specimens for histopathological and cytological examination were obtained from the stricture site. Different types of dilators were used. The patients were followed regularly and dilatation repeated if needed. Patients with strictures caused by malignancy underwent either radiotherapy or chemotherapy, or both. Few had surgery. Those with reflux esophagitis received antacids and H_2 receptor blockers.

The dilatation method was as follows. A forward-viewing gastroscope (diameter, 9-11 mm) was used along with different types of dilator devices. These included the savary, Maloney, Eder-Puestow, and pneumatic, as well as only the scope when appropriate. Dilatation is usually performed with the patients under intravenous diazepam or midazolam sedation. General anesthesia was used in only four patients, three of whom were children. Following initial endoscopic assessment of the stricture type, a suitable dilator was selected and used for dilatation. Generally three to four dilatations were performed per session, with an average increase in the diameter of the dilator device of approximately 2 to 4 mm. After the dilatations were performed, endoscopy was redone whenever possible for complete assessment of the stricture, length, presence of tumor, and postdilatation bleeding or other complications. Assessment of the stomach and duodenum was also done. In patients with tight strictures (less than 11 mm in diameter), dilatations were repeated every 3 to 7 days until a larger-diameter dilator device could be passed. If this was not possible, a feeding or Atkinson tube was inserted under fluoroscopic control. This was more necessary in patients with malignant strictures. Usually patients were dilated up to 18 to 20 mm until they became free of symptoms. If symptoms recurred, a repeated course of dilatations was performed. Different dilators were used, depending on the type of stricture. Pneumatic dilators were used usually in patients with achalasia. For patients with soft strictures or lower esophageal rings, Maloney dilators or a larger-diameter scope may be used to rupture the ring.

In patients with rigid strictures, Eder-Puestow or savary dilators were used with a guidewire and inserted sometimes under fluoroscopic control. Fluoroscopy was used in 16 patients who had a very tight or pinhole stricture, where the guide wire was passed into the stomach under fluoroscopic control and then the dilatation was performed. Fluoroscopy was also used in another six patients who underwent Celestin or Atkinson tube insertions.

Results

Between June 1982 and December 1988, 203 endoscopic esophageal dilatations were performed in 83 patients. The savary dilator was used in 114 cases; Maloney in 67; Eder-Puestow in 12; pneumatic in eight; and the scope only in two cases. There were 46 patients with benign strictures; 31 were males and 15 females. Their ages ranged between 2 and 75 (average, 31.1) years. Thirty-seven patients had malignant strictures caused by esophageal cancer; 35 were males and two females. Their age ranged between 44 and 90 (average, 68.3) years.

The etiology of benign strictures is shown in Table 1 (Figures 1 to 3) and of malignant strictures in Table 2. Postoperative benign esophageal strictures occurred because of esophageal transection in five patients; repair of hiatal hernia, four patients; and achalasia, two patients; and followed repair of congenital esophageal stricture in one. Five patients suffered esophageal strictures following resection for malignancies. The sites of strictures are shown in Table 3. The most common one occurred in the lower part of the esophagus. The number of dilatations ranged from one to 15, with most patients undergoing one procedure (N = 36) and only one undergoing 15 dilatations (Table 4). Seventeen patients (36.9%) with benign strictures became symptom free after one

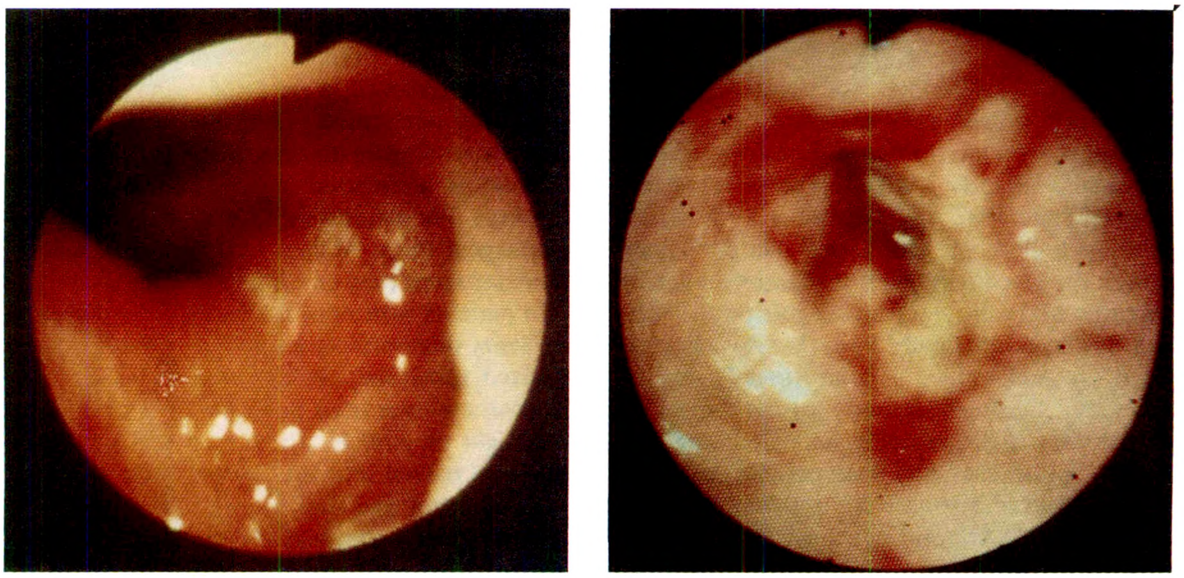


FIGURE 1. Hiatus hernia (left) causing some reflux esophagitis and esophageal stricture (right).

dilatation. Nineteen patients (51.4%) with malignant strictures had only one dilatation; 14 became asymptomatic and the other five required tube insertion for feeding before surgery, radiotherapy, or chemotherapy was carried out. Fifteen of these patients were newly diagnosed by endoscopy, 11 of whom later received radiotherapy or chemotherapy and four had surgery. After undergoing sclerotherapy, one patient suffered ulcerations and then stricture, which required 15 dilatations as the stricture was fibrous and rigid. Treatments extended over a period of 14 months, after which he remained asymptomatic for the remaining follow-up period of 2 years.

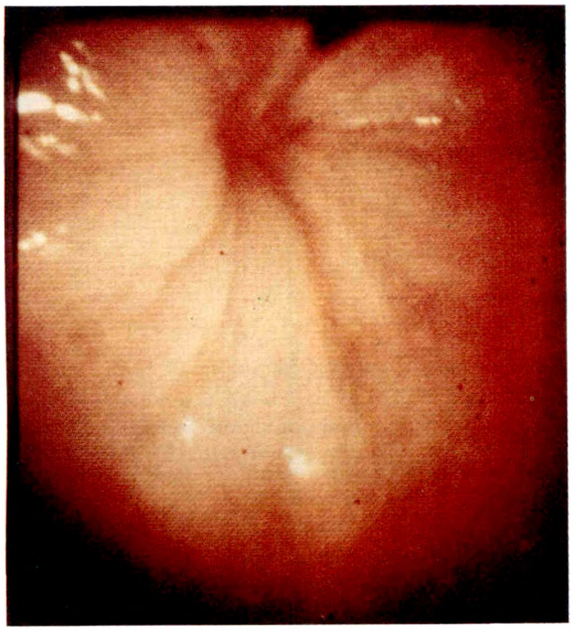
Tubes inserted to maintain adequate nutrition were as follows: feeding tubes in 14 (six for benign and eight for malignant strictures), Atkinson tubes in four patients with malignant strictures, and Celestin tubes in two patients with malignant strictures. Six patients with benign strictures had feeding tubes inserted during the first dilatation. Of 14 patients with malignant strictures five had tubes inserted during the first dilatations and nine had them inserted with the second or consecutive dilatations (Figure 4). Dilatation and tube insertion failed in four patients and they were referred for surgery: two had malignant strictures and two had benign strictures, one high esophageal stricture due to esophageal inlet patch[4] (Figure 5) and the other longstanding stricture caused by corrosives.[5]

TABLE 1. *Cause of benign strictures.*

Etiology	No. of patients	No. of dilatations
Postoperative	12	32
Esophagitis	15	32
Achalasia	5	10
Corrosives	4	12
Esophageal inlet patch	1	2
Congenital	4	8
Post sclerotherapy	1	15
Schatzki ring	1	1
Unknown	3	10
Total	46	122

The follow-up period for benign strictures from the time of the last dilatation ranged between 7 weeks and 53 months (average, 8.5 months) and for malignant strictures, between 2 weeks and 21 months (average, 2.3 months).

Minor complications following esophageal dilatation occurred in a few patients. Eleven had mild to moderate bleeding and two others suffered aspiration. Esophageal perforation occurred in one patient with malignant stricture during insertion of the Atkinson tube, and this healed with



conservative treatment. There was no mortality that could be directly attributed to the dilatations, and those deaths that did occur were usually due to the complications of malignancy or, in those patients with benign strictures, unrelated causes.

Discussion

Dilatation of esophageal strictures without surgical intervention has been successfully carried out since the early nineteenth century.[1] Endoscopic dilatation is safe[2,3] and carries less risk than surgery done under general anesthesia. The postoperative mortality and morbidity, especially in elderly patients, may be as high as 6%.[6] Strictures may later develop in patients who have esophageal surgery and will need endoscopic dilatation, as occurred in 17 (20.5%) of our patients. Endoscopic dilatation is a definitive treatment in patients with benign strictures, and this was

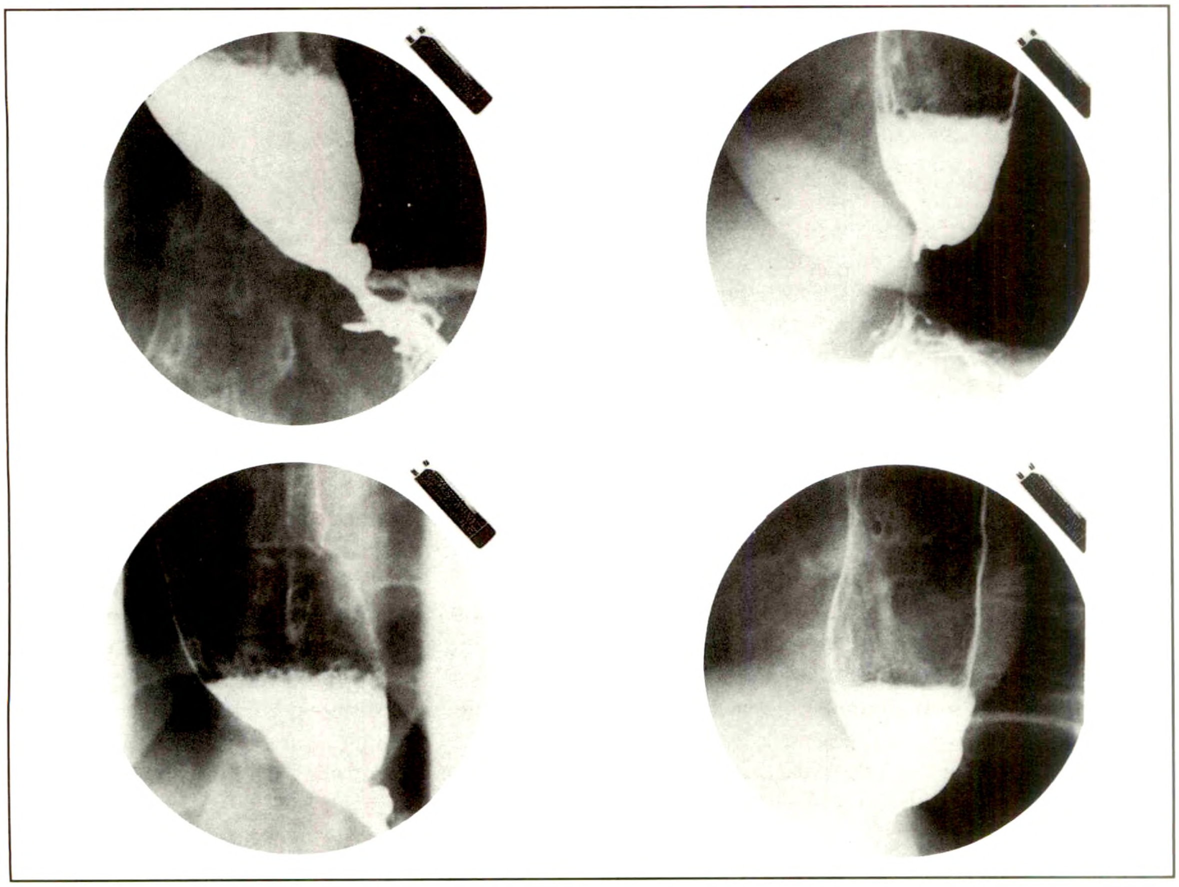


FIGURE 2. Endoscopic view and barium swallow showing achalasia.

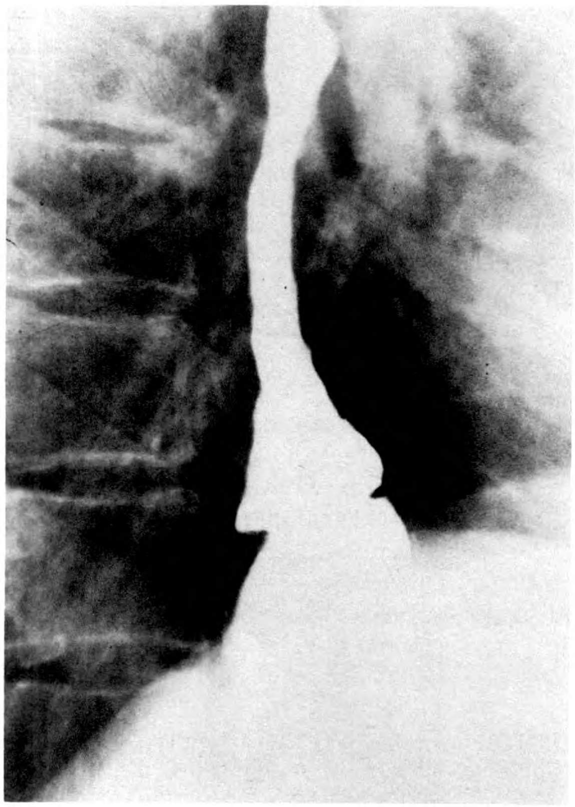


FIGURE 3. Barium swallow showing Schatzki ring.

TABLE 2. *Malignant strictures.*

Etiology	No. of patients	No. of dilatations
Postoperative	5	10
Post radiotherapy ± chemotherapy	16	41
Both	1	6
None	15	24
Total	37	81

TABLE 3. *Site of esophageal stricture.*

Site	Benign strictures (No. of patients)	Malignant strictures (No. of patients)
Upper	3(6.5%)	2(5.4%)
Middle	6(13.0%)	10(27.0%)
Lower	37(80.5%)	25(67.6%)

TABLE 4. *Number of dilatations.*

No. of dilatations	Benign strictures (No. of patients)	Malignant strictures (No. of patients)
One dilatation	17(36.9%)	19(51.4%)
Two dilatations	12(26.1%)	6(16.2%)
Three dilatations	7(15.2%)	5(13.5%)
> 3 dilatations	10(21.8%)	7(18.9%)

shown in our study in which over 78% of our patients with benign strictures became symptom free following one to three dilatations, with no recurrence during follow-up. Only one patient required 15 dilatations. This patient, who may also have had a secondary esophageal motility disorder, experienced improvement between dilatations. After the fifteenth dilatation, he required no further dilatation and became symptom free for more than 2 years. Dilatation failed in two patients who subsequently underwent surgery.

None of our patients with benign strictures suffered serious complications following dilatation. Carcinoma of the esophagus is one of the most common malignancies in Saudi Arabia.[7,8] In patients with malignant strictures, endoscopic dilatation is a good method for alleviating the dysphagia before or after chemotherapy, radiotherapy, or surgical treatment.[9] Dilatations that include insertion of feeding or Atkinson tubes allow for oral feeding and good nutrition, prevent inhalation, and improve the quality of life.[10]

Fiberoptic endoscopes allow for objective evaluation of the type and site of the stricture, and thus the selection of a suitable dilatator. Sufficient and repeated biopsy specimens can be taken from strictures through an endoscope, a guide wire can be inserted through a narrow stricture to facilitate dilatation, and feeding or other palliative tubes can be inserted under direct vision. Serious complications are rare; in our series, perforation developed in only one patient. Dilatations may be repeated at short intervals, if needed, to maintain adequate swallowing, and most can be managed on an out-patient basis, as was done in most of our patients with benign strictures.

Complications from endoscopic esophageal dilatation are recognized but rare, as esophageal perforation occurs in approximately one in every 400 dilatations.[11]

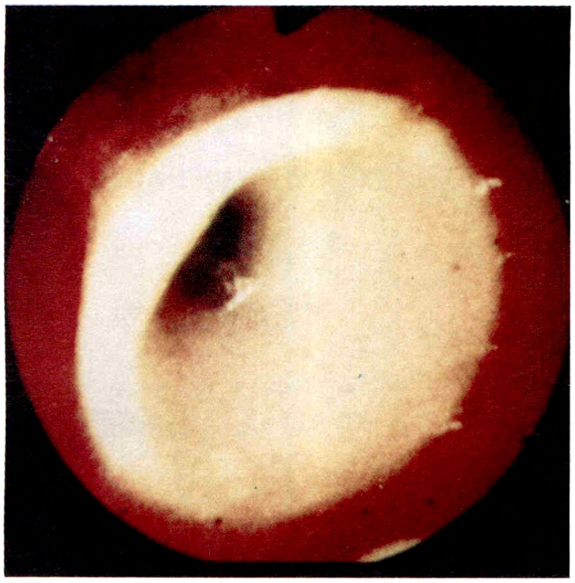


FIGURE 4. Atkinson tube inserted in a patient with carcinoma of the esophagus.

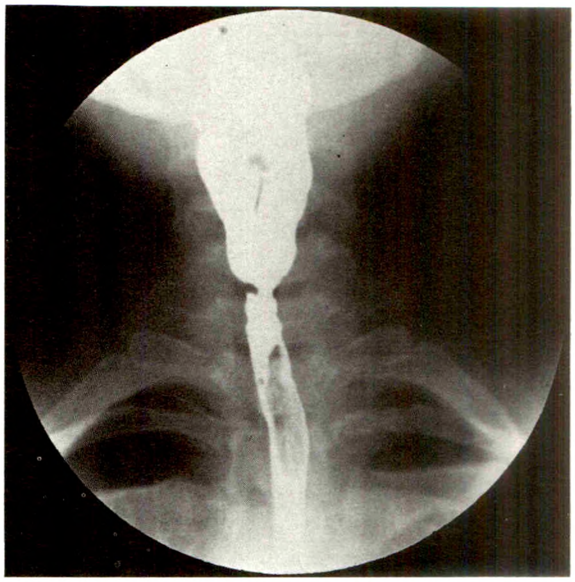


FIGURE 5. Barium swallow showing high esophageal stricture due to esophageal inlet patch.

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THE USUAL AND THE UNUSUAL PRESENTATION OF EWING'S SARCOMA

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أجرينا دراسة مراجعة لأربعة عشر (١٤) مريضا يعانون من غرن يوينغ المثبت بالتشخيص النسيجي بهدف تحليل السمات السريرية والشعاعية للمرضى كما شوهدت في مستشفى الملك خالد الجامعي ومقارنتها بالسمات المذكورة في الكتابات الطبية. كانت المجموعة تتكون من تسعة ذكور وخمس اناث، ومتوسط العمر ١١سنة. اشتكى جميع المرضى من تورم مؤلم ما عدا مريض واحد، ودامت الأعراض ٤أشهر في المتوسط، ووجدت قصة رضح لدى ٥٠٪ من المرضى. اختلف المظهر الشعاعي تبعا للعظم والجزء المصاب منه، ولم يشاهد المظهر المدرسي إلا لدى ٣٦٪ من المرضى فقط. وثبتت صحة التشخيص الموقت لغرن يوينغ بناء على النتائج السريرية والشعاعية في ٥٠٪ من الحالات. واشتملت التشخيصات الأخرى على التهاب العظم والنقي والرضح والغرن العظمي وداء الشُّعَيَّات. وبذلك يمكن أن يتشابه غرن يوينغ مع حالات متنوعة، ومع ان التشخيص يكون مؤكدا عند اقتران ظهور التورم المؤلم بالفحص السريري مع المظاهر الشعاعية لآفة متلفة في هيكل غير ناضج إلا أنه قد تحدث اختلافات عن السمات المعتادة.

We conducted a review of 14 patients with an established histological diagnosis of Ewing's sarcoma in order to analyze the clinical and radiological features of the disease as observed at King Khalid University Hospital and to compare them with those reported in the literature. There were 9 males and 5 females, and the average age was 11 years. All patients but one complained of a painful swelling. Symptoms had lasted an average of 4 months and 50% of the patients had a history of trauma. The radiological appearance varied according to the bone and the part of the bone involved. Only 36% of the patients exhibited the classic appearance. Based on the clinical and radiological findings, the provisional diagnosis of Ewing's sarcoma was accurate in 50% of the cases. Other diagnoses included osteomyelitis, trauma, osteosarcoma, and actinomycosis. Ewing's sarcoma may mimic a variety of conditions, and although a combination of painful swelling seen clinically and a destructive lesion shown radiologically in an immature skeleton should confirm the diagnosis, variations from the usual features do occur.

Ewing[1] in 1921 described a diffuse endothelioma of the bone that merited separate identification because of its diaphyseal localization, its uniform appearance, and its high sensitivity to radiation. Since then much has been written about this tumor and there is still controversy with respect to its individual characteristics, origin, and relationship to reticulosarcoma.[2-4]

This relatively rare tumor occurs most frequently in the second decade of life, with males more often affected than females.[2,5,6] Although any part of any bone may be affected,[4] a primary location in the epiphysis is unusual and the bones of the hands and feet with the exception of the calcaneus are only rarely involved.[3,4]

Clinically, pain and swelling of relatively short duration are the most common presenting symptoms.[3-5] Radiologically the lesions usually show a destructive appearance with extensive soft

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tissue invasion. The classic manifestation is that of a lesion in the medullary zone of the midshaft of a long bone with cortical destruction and multiple layers of new periosteal bone, giving an "onion skin" appearance.[3-5,7] Variations have been seen, and the radiological appearance varies according to the bone and/or part of bone involved.[3,4]

The aim of this review was to study and analyze the clinical and radiological features of Ewing's sarcoma as observed at King Khalid University Hospital, and then to compare our observations with those reported elsewhere in the literature.

Patients and Methods

Records of all patients with a histologically confirmed diagnosis of Ewing's sarcoma who were admitted to King Khalid University Hospital from 1983 to 1988 were reviewed. The data collected included age, sex, presenting complaint, duration of symptoms, history of trauma, clinical findings, radiological features, and provisional diagnosis.

Radiologically, the type of bone (long, flat, small), the part of the bone (epiphysis, metaphysis, diaphysis), the affected site (medullary, cortical), the appearance (destructive, osteoblastic), and periosteal reaction were noted and recorded. Computed tomograms of the lungs and technetium isotope bone scan were reviewed to evaluate the presence of metastases. The tumors were then grouped according to the following types:[3,4] central diaphyseal, metaphyseal, cortical, flat bones, and small bones.

Results

There were 14 patients: nine (64%) were males and five (36%) were females. Age ranged between 2 and 40 years (average, 11 years). All patients complained of painful swelling except one whose swelling was painless. Duration of symptoms ranged between 2 and 8 months (average, 4 months), and there was a history of trauma in 50% of the cases.

Clinically, the large swelling was firm to hard in 11 cases and cystic to soft in three. Long bones were involved in 72% (femur 6, humerus 3, fibula 1), flat bones in 21% (pelvis 2, scapula 1), and small bones in 7% (calcaneus 1).

Based on the radiological appearance, the tumors were grouped according to the bone or part of the bone involved:[3,4]

1. Central diaphyseal: The classic appearance was seen in 5 cases (36%); the point of origin was within the medullary canal and the tumor was expansile and osteolytic with a lamellar periosteal reaction (onion skin appearance) (Figure 1).
2. Metaphyseal: Three cases (21%) were noted. The point of origin was in the metaphysis, and the tumor was destructive with ill-defined borders. In one case the destruction involved the epiphysis and the remainder of the bone showed sclerosis and periosteal reaction (Figure 2).
3. Cortical: Two cases (14%) were of this type and showed partial subperiosteal cortical necrosis, asymmetrical expansion, and invasion of soft tissue (Figure 3).
4. Flat bone: Three cases (21%) involved the flat bones. One showed almost complete destruction of the scapula (Figure 4) with

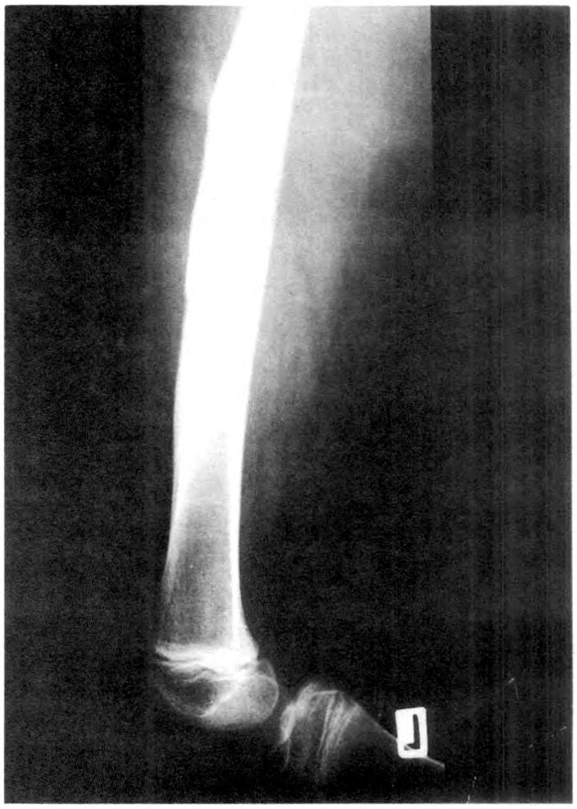

FIGURE 1. X-ray study of femur showing a central diaphyseal type of Ewing's sarcoma.

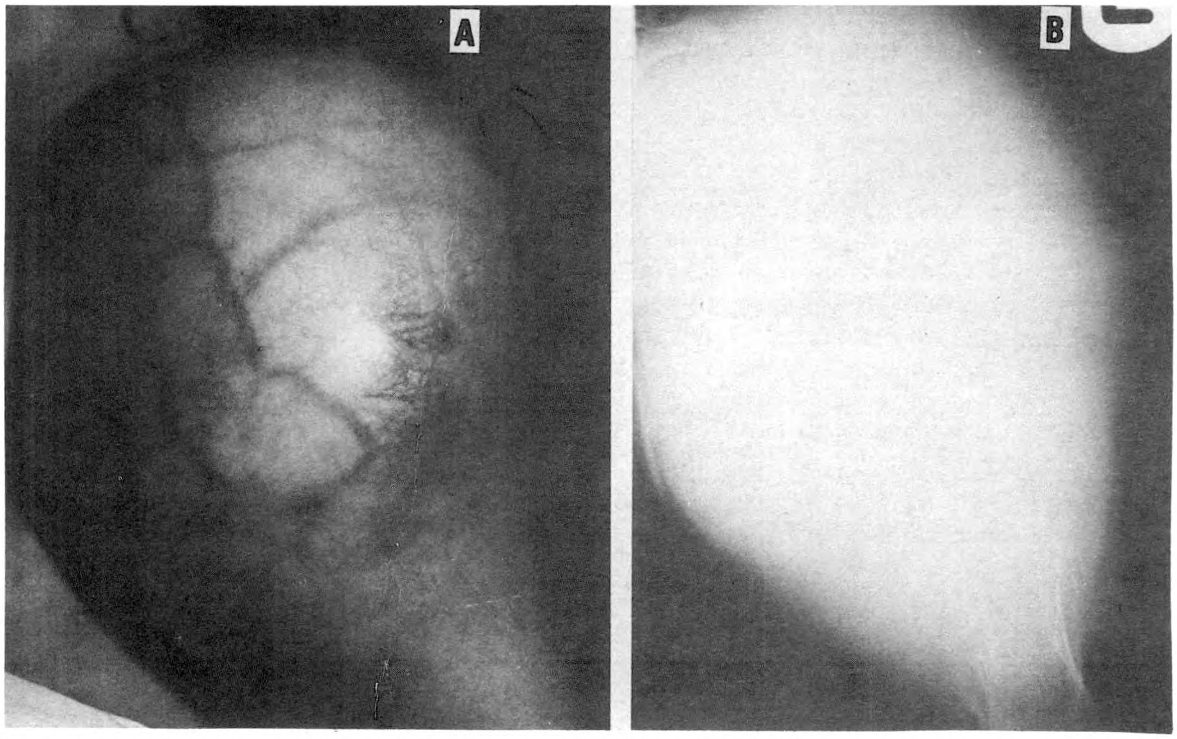

FIGURE 2. (A) The arm of a 2-year-old girl admitted with a painful swelling of 4 months' duration. (B) X-ray study showing destruction of the proximal half of the humerus.

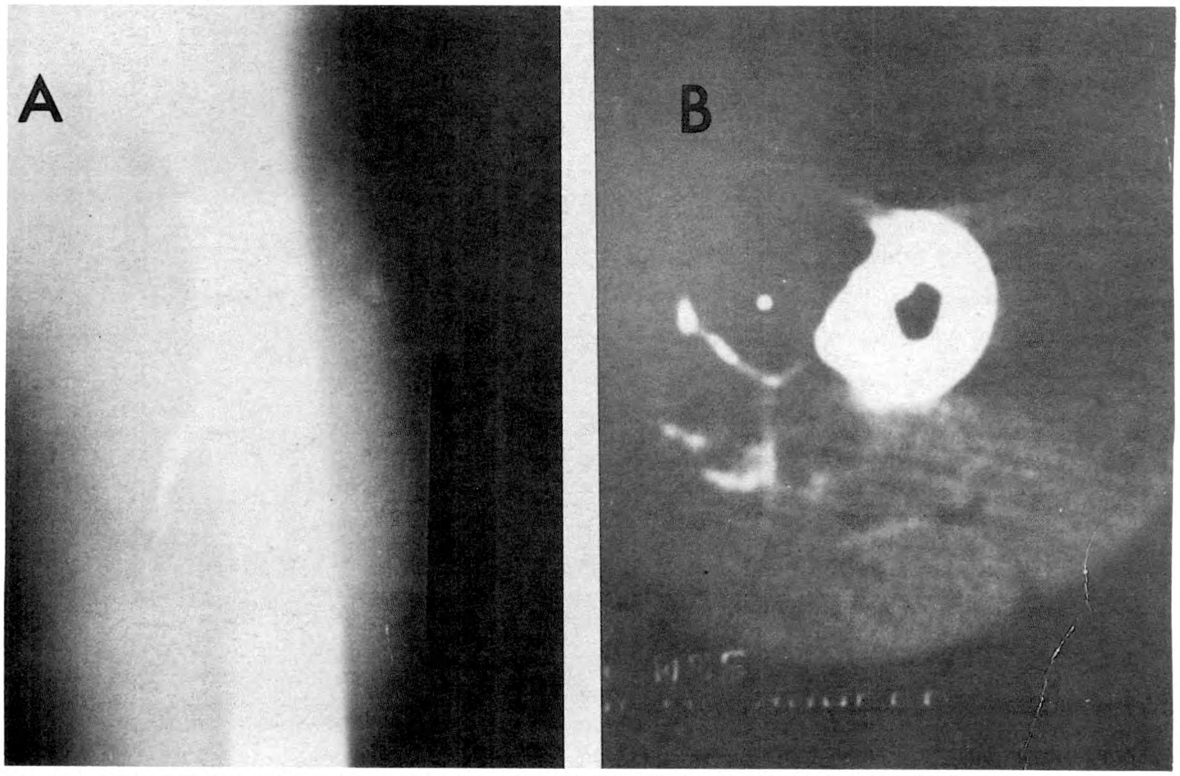

FIGURE 3. (A) X-ray study and (B) computed tomographic scan of femur showing the cortical type of appearance.

no periosteal reaction and the remaining two which involved the pelvis showed areas of osteolysis and decreased density.

5. Small bones: Only one case (7%) was seen and this occurred in the calcaneus. Radiologically it resembled actinomycosis. There were signs of marked porosis of the foot bones, a huge soft tissue mass, and sclerosis of the calcaneus (Figure 5).

Four of our patients (28.5%) showed a radiologically detectable metastasis in the lungs. Based on clinical and radiological findings, the provisional diagnoses of the 14 cases were as follows: Ewing's sarcoma, 7 (50%); osteomyelitis, 3 (21.5); trauma, 2 (14.5%); osteosarcoma, 1 (7%); and actinomycosis, 1 (7%).

Discussion

It has long been recognized that pain and swelling of relatively short duration are the most common presenting symptoms in Ewing's sarcoma and the tumor shows a male predilection.[2-5] This has been confirmed by the present study in which

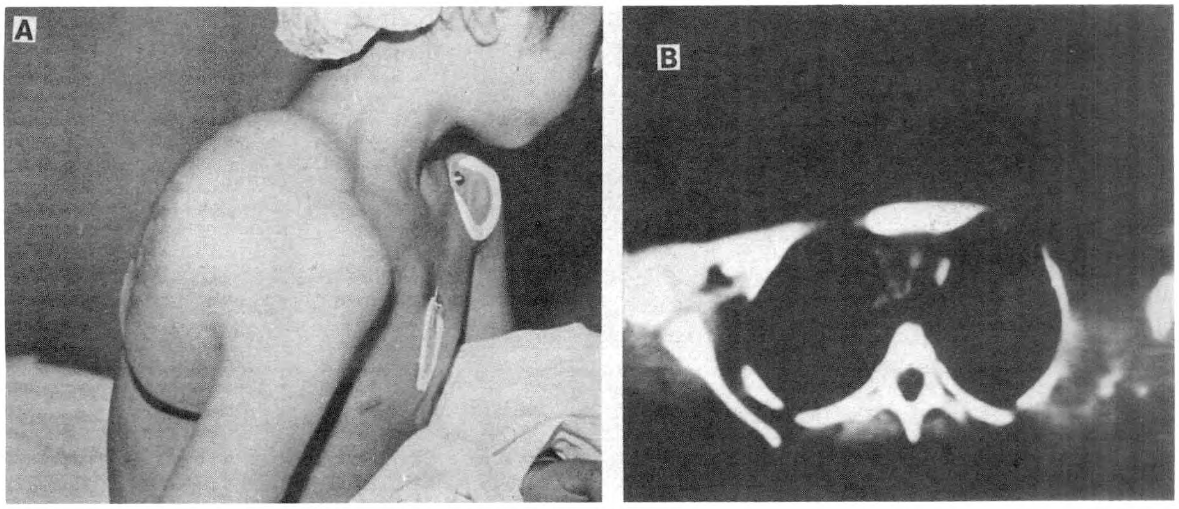

FIGURE 4. (A) A 9-year-old girl admitted with a painful swelling in the scapular region of 4 months' duration. (B) Computed tomographic scan showing almost complete destruction of the scapula.

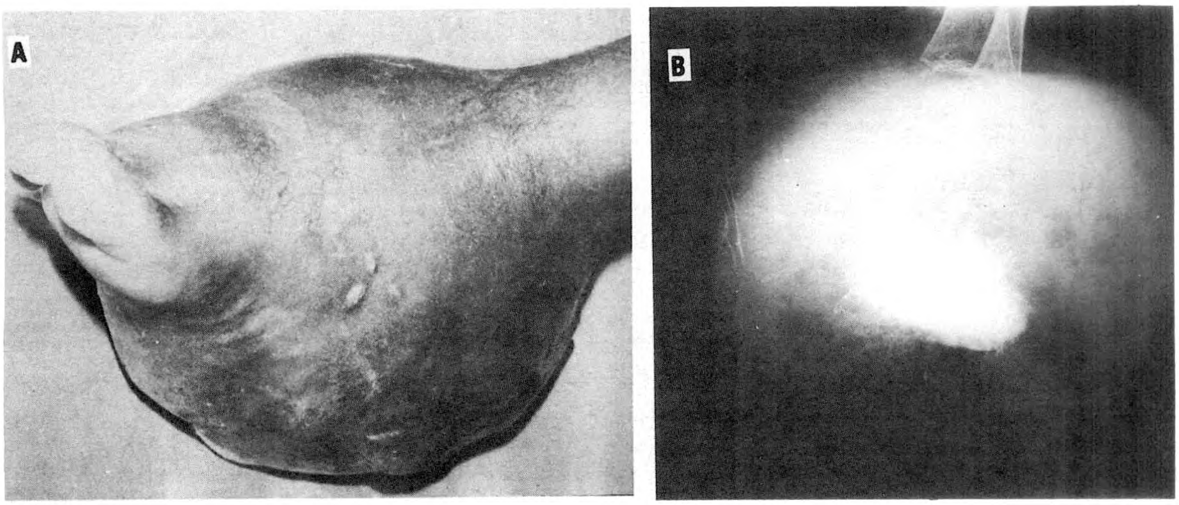

FIGURE 5. (A) The foot of a 12-year-old boy who was admitted with a painful swelling of 8 months' duration. (B) X-ray study showing sclerosis of the calcaneus, soft tissue mass, and porosis of the other foot bones.

all but one patient complained of a painful swelling, males outnumbered females by 1.8 to 1, and the duration of symptoms averaged 4 months.

The tumor occurs most commonly in the immature skeleton, with the majority of patients between 5 and 14 years of age,[3] but variations do occur.

Ridings,[8] in a review of the literature, found that the youngest patient was 7 months old. Aegerter and Kirkpatrick[4] stated that the tumor occurs rarely in patients over age 30. In the present series the youngest patient was 2 years old and the oldest was 40. The skeletal location of Ewing's sarcoma is not as precise as with most other bone tumors[4] and the radiographic findings are not uniform.[3]

Long bones are most commonly involved. Aegerter and Kirkpatrick[4] reported that long bones were affected in two thirds of the cases and that flat bones are affected in the remaining one third. Among the long bones, the diaphysis is the most frequent site of origin and an epiphyseal primary location is rare.[3,4] Almost 72% of our cases occurred in the long bones, 21% in flat bones, and 7% in small bones. In the cases occurring in the long bones, 50% were central diaphyseal, 30% metaphyseal, and 20% cortical.

The radiological appearance seems to vary according to the bone or part of bone affected. The classic appearance has been observed in 25% of the cases.[4] In our series it was seen in 36% of the cases, all of which were the central diaphyseal type. The metaphyseal type of Ewing's sarcoma is usually extensive, originating at a metaphyseal or metaphyseodiaphyseal point, and reaching toward the diaphysis. It commonly has ill-defined borders but seldom invades the epiphysis, and its appearance may be purely lytic or may combine lytic and sclerotic features.[3] It is rare for the tumor to involve the epiphysis but did in one case in our series. The tumor destroyed the proximal half of the involved bone including the epiphysis, and the remainder of the bone showed sclerosis and periosteal reaction.

The diaphyseal cortical type is characterized by subperiosteal cortical erosion, asymmetrical development, and soft tissue invasion,[3,4] a finding noted in the two cases of this type in our series.

The flat bones and small bones when affected usually show signs of osteolysis with little or no periosteal reaction. The three cases involving flat bones in our series did not differ in appearance from that reported by others[3,4] but in one case in which the calcaneus was involved the bone showed marked sclerosis (Figure 5).

No single clinical or radiological finding seems to be pathognomonic of Ewing's sarcoma, and the tumor can mimic a variety of conditions such as osteomyelitis, eosinophylic granuloma, and osteosarcoma.[3,4] In the present series the provisional diagnosis was accurate in only half of the cases; other possible diagnoses included osteomyelitis, trauma-induced osteosarcoma, and actinomycosis.

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Special Communication

BLOOD COAGULATION AND THE NEPHROTIC SYNDROME: DEFICIENCY OR EXCESS?

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قد تضطرب عملية الارقاء الطبيعي في مرضى المتلازمة الكلائية. تحدث عادة زيادة في قابلية الدم للخثار، إلا أن هنالك تقارير متفرقة عن حدوث نزف غير عادي. تنجم هذه الاضطرابات فيما يبدو عن فقدان غير عادي للبروتين أو نقص البومين الدم أو فرط شحوم الدم وكلها مميزات لحالة المتلازمة الكلائية. تتضافر عوامل متعددة في التهيئة للمضاعفات الخثارية مثل تركز الدم وزيادة تكدس الصفيحات وتزايد نشاط العديد من عوامل التخثر بالاضافة إلى عيوب إنحلال الفيبرين. ويحصل الاستعداد للنزف عادة عن نقص مكتسب في بعض عوامل التخثر.

Normal hemostasis can be disrupted in patients with nephrotic syndrome. More commonly a thrombotic diathesis is seen but there are also sporadic reports of abnormal bleeding. These abnormalities appear to result from the abnormal protein loss, hypoalbuminemia, and hyperlipidemia that characterize the condition. Hemoconcentration, enhanced platelet aggregation, increased activity of several coagulation factors, and defective fibrinolysis collectively predispose to thrombotic complications. An acquired deficiency of some clotting factors is usually responsible for the bleeding diathesis.

Patients with nephrotic syndrome tend to suffer from a spectrum of hemostatic disorders, ranging from an increased incidence of thromboembolism to an increased bleeding tendency.[1-3] Although the association between nephrotic syndrome and thromboembolic complications has been recognized for more than a century, the precise causal relationship is not entirely understood.[4-6] Moreover, the association between the increased bleeding tendency and nephrotic syndrome is also somewhat unclear.[2-7] In this review, we present a current synopsis on the subject and discuss some of the controversial aspects that have emerged during the past decade.[8,9] An in-depth understanding of the underlying pathogenesis should pave the way to better clinical methods for preventing these grave complications.

In discussing the diverse hemostatic abnormalities associated with the nephrotic syndrome, it is preferable to divide these abnormalities into two categories: first, alterations that predispose to a hypercoagulable state, and second, abnormalities that lead to a bleeding tendency (Table 1).

Factors Predisposing to a Hypercoagulable State

It is well known that the thromboembolic complications seen in the nephrotic syndrome are preceded by a hypercoagulable state which until recently has proved relatively difficult to diagnose, largely due to lack of reproducible techniques for detecting and monitoring the various changes in the coagulation cascade.[10,11] It is known that there is a major biochemical imbalance between procoagulant and anticoagulant mechanisms in the presence of a hypercoagulable state. The precise pathophysiology has recently been summarized by Bauer and Rosenberg[9] and is beyond the scope of this review. Pursuant to this and other observations, it was discovered that four major abnormalities can lead to a hyper-

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TABLE 1. *Factors with potential to affect hemostasis in the nephrotic syndrome.*

Abnormal bleeding	Thrombotic tendency
Decreased platelet	Increased blood viscosity
Adhesion	
Aggregation	Enhanced platelet
Release	Adhesion
	Aggregation
Decreased level or activity of coagulation factors	Release
Decreased synthesis	
Abnormal urinary losses	Increased level or activity of coagulation factors
Abnormal inhibitors	Increased synthesis
	Abnormal urinary losses of inhibitors (antithrombin III, protein C)
Increased fibrinolysis	
Enhanced activation of plasmin	Increased level of activators
Deficient inhibition of plasmin	
	Decreased fibrinolysis
	Deficient activation
	Enhanced inhibition

coagulable state, with its dire consequences. These are: (1) profound abnormalities in the coagulation cascade with substantial alterations in zymogens and co-factors; (2) alterations in the coagulation inhibitors; (3) alterations in the fibrinolytic system; and (4) defects in the molecular functions of platelets.

Zymogens and Co-Factors

Among the zymogens of patients with nephrotic syndrome, most investigators have demonstrated decreased plasma concentrations of factors II, VII, IX, XII, and XIII.[2,5,12-15] Conversely, increased plasma concentrations of co-factors I, V, and VIII have also been consistently observed in other studies.[16,17] Alterations in other zymogens such as factor X remain controversial, with some investigators reporting an increase and others a decrease or no change in the plasma levels.[16,18] It is generally assumed, but without major supportive evidence, that such elevated plasma levels of zymogens and co-factors are usually caused by an increased rate of synthesis or, perhaps, a decreased volume of distribution.[19]

Coagulation Inhibitors

Several components of the coagulation inhibitors have been found to be altered in the nephrotic syndrome. The major inhibitors appear to be antithrombin III, protein C, and protein S.[20-24] Antithrombin III appears to be the most important and perhaps the best studied. It is the principal inhibitor of thrombin, activated factors IX, X, XI and XII, and plasmin.[25,26] More than 90% of patients with nephrotic syndrome and documented thromboembolic phenomena have been shown to have antithrombin III levels that are less than 75% of normal.[20] The mechanism responsible for the subnormal serum or plasma levels of this protein has not yet been clarified. Because antithrombin III has been detected in the urine of nephrotic patients,[26] it is conceivable that either increased urinary losses or enhanced renal tubular catabolism of this protein could play an important role in this regard.

Although an increased in vivo consumption of antithrombin III by an ongoing generation of thrombin may also reduce its concentration, at least one study[20] has not revealed any further reductions in the serum antithrombin III levels after the development of venous thrombosis, therefore excluding such a possibility. To date, there have been no studies addressing the possibility of a reduced rate of synthesis of antithrombin III in patients with the nephrotic syndrome.

Recently the importance of two other coagulation inhibitors has been recognized. A deficiency of activated protein C, normally an inhibitor of co-factors V and VIII, was noted to have a role in the thrombotic tendency observed in a familial protein C deficiency state.[27] It was found that a protein C level below 50% resulted in an increased tendency to thrombosis. It has since been well established that activated protein C and antithrombin III activity are complementary.[28] The precise alteration of protein C in patients with nephrotic syndrome remains unclear, with some studies demonstrating an increased urinary loss of this glycoprotein while others have shown significantly higher levels than those seen in controls.[23,24] It has also been noted that the activity of protein S, a plasma protein that normally serves as a co-factor for activated protein C, may also be compromised in patients with nephrotic syndrome. Some studies have recently shown that the levels of free protein S are significantly reduced in nephrotic patients, resulting in an increased predisposition to thrombosis.[23,29]

Fibrinolysis

Dysfunction of the fibrinolytic system may also be involved in the various mechanisms contributing to the disordered hemostatic process observed in the nephrotic syndrome. The regulatory role of the generation of plasmin in the coagulation process is suggested by the known actions of plasmin in degrading not only fibrin, but also fibrinogen and factors V and VIII.[30] These effects may help to localize the thrombus to the site of vascular injury.

The conversion of plasminogen to plasmin requires the presence of activators. The nature of such activators is unknown, although kallikrein, activated factor XII, protein C, and other tissue or endothelial factors may constitute some of them.[31] Unlike plasma, for which the activity of plasmin is readily neutralized by alpha$_2$-antiplasmin, alpha$_2$-macroglobulin, alpha$_1$-antitrypsin, and other inhibitors, the in vivo activation of plasmin in the matrix of the thrombus wall[8,32] generally results in a locally uninhibited fibrinolysis. Therefore, if the activators are deficiently released or the inactivators abnormally increased, the hemostatic process could be disturbed. The latter may in turn predispose to either the inefficient removal of an already formed thrombus or to an inappropriate inhibition of the clotting process. Several abnormalities of the fibrinolytic process have been described in patients with nephrotic syndrome.[19,33-35] It appears that, except for one report, the most consistent pattern has been decreased fibrinolytic activity.[5,17,34,35] The mechanism, or mechanisms, leading to decreased fibrinolysis remain uncertain. Defective formation or release of plasminogen activator, or an increase in antiplasmin activity, or both mechanisms, have been suggested.[34,35] Abnormal urinary losses of plasminogen activators, or the presence of abnormal inhibitors of these activators, could similarly contribute to such an abnormality.

Physical exercise is known to result in increased fibrinolytic activity of blood after venous occlusion,[36] an effect not usually observed in hyperlipidemic subjects.[37] It is therefore possible that nephrotic individuals who are sedentary and frequently hyperlipidemic could have similar reductions in the release of plasminogen activator. One preliminary study documented such a deficient activator release after venous occlusion in nephrotic patients.[38]

Findings suggesting an increased rather than decreased fibrinolytic activator release have also been reported.[5] These conflicting reports may reflect variations in the degree of in vivo depletion of endothelial stores of the activator by an ongoing activation of coagulation factors or platelets. In this regard, the increased platelet aggregability along with the activation of coagulation factors described in nephrotic patients could promote a relative depletion of activators from endothelial cells,[39] thereby explaining such a variability. It is also conceivable that the lack of appropriate identification of the fibrinolytic events might well be related to technical inadequacies in the currently available laboratory methods.

Several other studies have also documented an increased inhibition of plasmin in the basal state, after venous occlusion, or both.[5,8,34] Only one study actually disclosed opposite findings.[17] This contradictory report can probably be explained by the fact that it documented a marked urinary loss of alpha$_1$-antitrypsin and an inadequate increase in the plasma concentration of alpha$_2$-macroglobulin. Since the above-mentioned proteins are important inhibitors of plasmin,[32,40] their deficiency could, therefore, lead to a lack of inhibition of the enzyme.

Platelet Function

The alterations in platelet-vascular interactions and the consequental propensity to develop thrombosis have been well described. Recently some studies described in depth the pathophysiological changes underlying these interactions and the function of arachidonic acid metabolites, the prostaglandins, and thromboxane in the regulation of such interactions.[9,41]

Thrombocytosis is often present in patients with nephrotic syndrome.[6,42] Although thrombocytosis in itself may not predispose to an enhanced platelet-vessel wall interaction, in vitro evidence indicates that platelets from patients with nephrotic syndrome frequently show an increased tendency to adhere, aggregate, and release their contents.[9,42,43] Findings from additional clinical studies have also suggested that platelet aggregation and the release reaction appear to occur in vivo, as reflected by an increased plasma level of beta-thromboglobulin and platelet factor IV, respectively.[43,44] In addition, nephrotic patients with renal vein thrombosis displayed a more accentuated tendency for in vitro and in vivo platelet aggregation compared to those without thrombosis. During remission of the nephrotic proteinuria, such enhanced parameters of platelet function have been noticed to return to the normal range,[44] suggesting an important relationship between the abnormal losses of protein and platelet behavior (vide infra).

The various factors responsible for such increased platelet adhesion and aggregation have not been definitely clarified. Because the adhesion of platelets to the subendothelial structures requires the binding of von Willebrand factor to a platelet receptor, it is possible that the high levels of factor VIII observed in patients with nephrotic syndrome could be responsible for promoting the initial attachment of platelets to the subendothelial structures.[5] In addition, it appears that the presence of hyperlipidemia and hypoalbuminemia may also be pathogenetically important. In this regard, increased plasma levels of beta-thromboglobulin and platelet factor IV have been documented in hyperlipidemic patients compared to age-matched and sex-matched normolipidemic control subjects.[45] Given the fact that cholesterol has been shown to enhance the production of thromboxane A_2 by the platelets,[46] it is conceivable that the accentuated platelet aggregation and release observed in hyperlipidemic subjects, including nephrotic patients, is caused by an increased rate of thromboxane A_2, and/or endoperoxide, generation by the platelets. This, in turn, may be a consequence of an alteration in the platelet membrane cholesterol-phospholipid ratio precipitated by the hyperlipidemia.[47]

In patients with cirrhosis and nephrotic syndrome, the presence of hypoalbuminemia has also been shown to be associated with an exaggerated platelet aggregation and release reaction.[44,48] These proaggregatory effects of hypoalbuminemia could, therefore, be synergistic with those resulting from the hyperlipidemia. The abnormal platelet activation caused by hypoalbuminemia can be prevented or corrected by the normalization of the plasma albumin level, or by simply adding albumin to plasma either in vitro or in vivo.[6,41,49] The mechanism, or mechanisms, leading to such an enhanced platelet aggregation as a result of hypoalbuminemia still remain unexplained. There is, however, some evidence to indicate that the abnormal platelet behavior might be caused by an increased rate of endoperoxide and thromboxane A_2 production by the platelets.[50] In this regard, the release of ^{14}C-labeled arachidonic acid from platelet membranes and its subsequent conversion to endoperoxides and thromboxane A_2 is apparently stimulated by a low albumin concentration, while it is inhibited by a normal albumin level.[41,51]

Because albumin will naturally bind the arachidonic acid that is released from platelets,[41,52] thereby preventing its subsequent metabolic degradation by means of platelet cyclooxygenase, the low albumin levels observed in nephrotic patients could make more arachidonic acid available for thromboxane A_2 or endoperoxide generation by the platelets.[41] In addition, because beta-thromboglobulin released from platelets during aggregation has been reported to inhibit prostacyclin I_2 production by endothelial cells, it is possible that an acquired deficiency of this autacoid could also contribute toward maintaining the hyperaggregatory state.[53] Furthermore, the aggregated platelets usually express factor XI-like activity in their membranes and provide a substrate for the activation of factors XII, X, and V.[42] These latter actions may also be synergistic with the effects of hypoalbuminemia and hyperlipidemia in promoting or supporting a hypercoagulable state in nephrotic patients.

Blood Viscosity

Some patients with nephrotic syndrome and a normal hematocrit have displayed increased in vitro red cell aggregation caused by the high fibrinogen concentration in their plasma.[54] This high fibrinogen concentration can cause an increase in the blood viscosity and reduce the rate of blood flow through the blood vessels, particularly the veins.[54] In addition, the venous stasis can result in local hypoxemia, which in turn can lead to endothelial cell damage and disruption of the lining, with subsequent surface-mediated platelet activation and formation of a platelet plug.[55] The recent observation of a reduced red blood cell surface change in nephrotic patients may also be contributory.[56] Together these factors can provoke circumstances favorable for the formation of a thrombus.

Factors Favoring a Bleeding Tendency

Abnormal bleeding in nephrotic patients who are uremic may not be uncommon, but it is exceedingly rare to witness an increased hemorrhage tendency in the nonuremic nephrotic patient.[19] The principal factors favoring such an eventuality include decreased concentration or activity of some plasma coagulation cascade factors, as well as thrombocytopenia, which can rarely occur.[6] Furthermore, it is possible that the vascular production of prostacyclin I_2 is increased, while the production of thromboxane A_2 decreases, resulting in an increased bleeding tendency.[9]

The reduced plasma levels of the coagulation factors, in particular II, V, VII, IX, and XII, have already been discussed in detail. Defects of adenosine diphosphate-induced platelet aggregation and platelet factor III availability have also been noted.[9] With the exception of a reported case of severe deficiency of factor VII, which resulted in a prolonged prothrombin time and associated spontaneous subcutaneous and muscle hematomas,[2] most other deficiencies reported have been characterized by an asymptomatic prolongation of the prothrombin time or partial thromboplastin time.[13,14,19]

Pathophysiological Hypothesis

Based on the available evidence, the thrombotic tendency observed in patients with nephrotic syndrome could result from a combination of several procoagulant alterations, such as hemoconcentration, increased platelet function, enhanced activity of coagulation factors, and reduced fibrinolysis (Figure 1). The abnormal permeability of the glomerular filtration membrane is not only responsible for the increased urinary losses of albumin, but also for the escape of antithrombin III, protein C, protein S, and plasminogen activator from the circulation. The increased urinary losses of the latter could contribute to a defective inhibition of thrombin and the activated

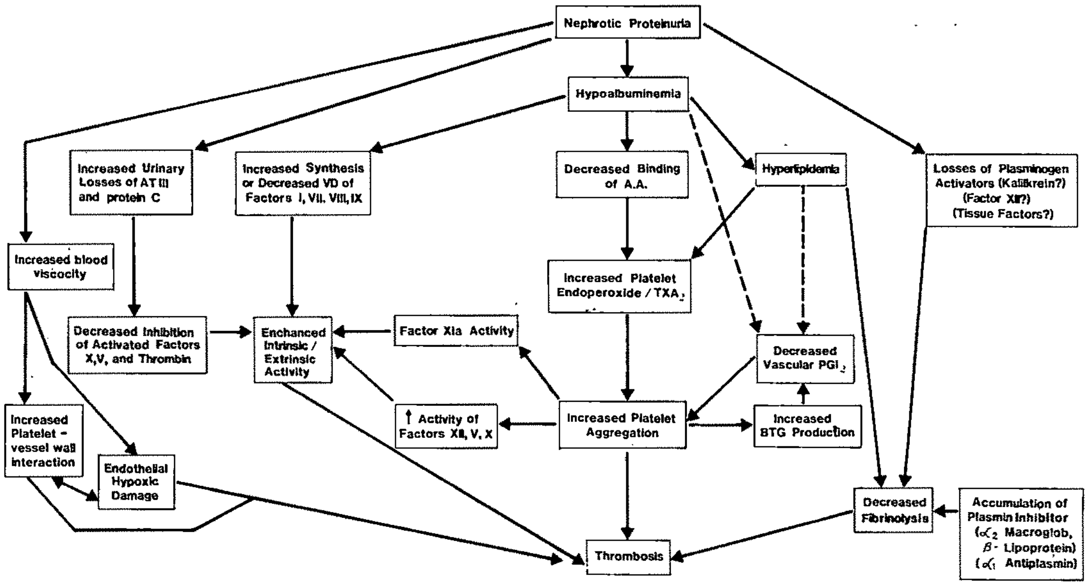
Nephrotic Proteinuria
Hypoalbuminemia
Increased Urinary Losses of AT III and protein C
Increased Synthesis or Decreased VD of Factors I, VII, VIII, IX
Decreased Binding of A.A.
Hyperlipidemia
Losses of Plasminogen Activators (Kallikrein?) (Factor XII?) (Tissue Factors?)
Increased blood viscocity
Increased Platelet Endoperoxide / TXA₂
Decreased Inhibition of Activated Factors X, V, and Thrombin
Enchanced Intrinsic / Extrinsic Activity
Factor XIa Activity
Decreased Vascular PGI₂
Increased Platelet - vessel wall interaction
↑ Activity of Factors XII, V, X
Increased Platelet Aggregation
Increased BTG Production
Endothelial Hypoxic Damage
Decreased Fibrinolysis
Accumulation of Plasmin Inhibitor (α₂ Macroglob, β- Lipoprotein) (α₁ Antiplasmin)
Thrombosis

FIGURE 1. Probable pathogenesis of the thrombotic tendency in the nephrotic syndrome. ATIII = antithrombin III; VD = volume of distribution; AA = amino acids; TXA_2 = thromboxane A_2; PGI_2 = prostaglandin I_2; BTG = beta-thromboglobulin.

forms of factors V and X, while the escape of antithrombin III could lead to a decreased fibrinolysis. In addition, the hypoalbuminemia that usually develops as a result of the abnormal proteinuria could simultaneously lead to enhanced platelet aggregation, a reduced volume of distribution of several coagulation factors, and hyperlipidemia. These three conditions in turn could further enhance platelet aggregation and the fibrinolytic defect. At the same time, the aggregated platelets could facilitate activation of the coagulation cascade, and by means of the release of beta-thromboglobulin, impair vascular prostacyclin I_2 production, thereby leading to defective control of the platelet procoagulant properties. Hemoconcentration can similarly predispose to local thrombosis by inducing venous stasis and endothelial damage.

Finally, the accumulation of plasmin inhibitors, such as alpha$_2$-macroglobulin and beta-lipoprotein, could also bring about further impairment of the plasma fibrinolytic activity. Whether hypoalbuminemia and hyperlipidemia are responsible for a decrease in vascular prostacyclin synthesis (PGI_2) remains to be demonstrated.

Conclusion

The nephrotic syndrome has occasionally been associated with a deficiency of factors II, VII, IX, XII, and XIII. Although these abnormalities were frequently asymptomatic (factors IX and XII), very rarely spontaneous bleeding (factor VII) occurred. In general, a spontaneous or steroid-induced remission of the nephrotic proteinuria has usually resulted in a resolution of such abnormalities. When surgical procedures, including renal biopsy, are contemplated in cases of severe deficiency, specific replacement therapy could be instituted.

More frequently, however, nephrotic patients are at risk or actually suffer thromboembolic phenomena. A combination of enhanced platelet aggregation, procoagulant changes in the clotting cascade, and decreased fibrinolytic activity is usually responsible. The risk of thrombotic complications seems to vary in direct proportion with the degree of proteinuria, hypoalbuminemia, and hyperlipidemia. There seems to be no specific factor, or factors, that identify patients at risk of thromboembolic phenomena, but sedentary activity, hemoconcentration, severe edema, and hyperlipidemia may constitute some of them. Although no prospective studies have yet been done, agents that inhibit thromboxane A_2 synthesis (e.g., aspirin) or that stimulate prostacyclin I_2 synthesis (e.g., dipyridamole) could constitute a potential prophylaxis against recurrence in high-risk patients.

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Clinical Review

HYPERLIPIDEMIA IN DIABETES MELLITUS: PATHOGENESIS, DIAGNOSIS, AND PHARMACOLOGICAL THERAPY

Klaus Johansen, MD

أشارت نتائج الدراسات الوبائية بصورة جلية إلى أن معدل الوفيات والمراضة لدى مرضى السكري يتجاوز ما يقابله لدى غير المصابين بداء السكري بمقدار الضعفين إلى ثلاثة أضعاف، بسبب احتشاء عضلة القلب، والسكتة الدماغية، والتصلب العصيدي للساقين. وعلى الرغم من أن نقص تحمل الغلوكوز يعتبر منفردًا ذا صلة باعتلال الأوعية الكبيرة، فقد تزايد الاهتمام في السنوات الأخيرة بالتركيز على دور البروتين الشحمي في الإصابة بالتصلب العصيدي لدى مرضى السكري. يتناول هذا التقرير التغيرات في تركيز الشحوم والبروتين الشحمي، والتقييم التشخيصي وعلاج الاضطرابات الشحمية في مرضى السكري.

Epidemiological studies have clearly shown that in diabetic patients there is a two to three times higher mortality and morbidity resulting from myocardial infarction, stroke, and atherosclerosis of the legs than in the nondiabetic population. Although decreased glucose tolerance per se is associated with macroangiopathy, in recent years increasing attention has been focused on the role of lipoprotein in the pathogenesis of atherosclerosis in diabetic subjects. This report describes changes in lipid and lipoprotein concentration, the diagnostic evaluation, and the management of lipid disorders in diabetic subjects.

Long-term diabetes is associated with an increased prevalence of atherosclerosis[1,2] which is the most common complication associated with long-term diabetes in the Western world. The increased cardiovascular morbidity and mortality in diabetes has naturally been related to the high prevalence of hyperlipidemia in the disease.[3-6]

Lipoproteins and Lipid Transport

Lipoproteins are high-molecular-weight globular particles that transport nonpolar lipids through plasma. Each lipoprotein contains a nonpolar core in which molecules of hydrophobic lipid are packed to form an oil droplet. The core consists of triglycerides and cholesteryl esters in varying proportions. A polar surface coat of phospholipid surrounds the core. The coat stabilizes the lipoprotein particle so that it can remain in solution in plasma. Each lipoprotein particle contains specific proteins, apoproteins, that are particularly exposed at the surface. The apoprotein binds to specific enzymes or transport proteins on cell membranes, thus directing the lipoprotein to its sites of metabolism. There are five major classes of lipoproteins (chylomicrons, very-low-density lipoprotein [VLDL], remnants, low-density lipoprotein [LDL], and high-density lipoprotein [HDL]), which differ in the composition of the nonpolar lipids in the core, in the composition of the apoprotein (A, B, C, E), and in the density, size, and electrophoretic mobility.

Triglycerides and cholesterol from food are incorporated into large lipoprotein particles, chylomicrons, in the intestines which pass by means of the lymph system into the general circulation for subsequent transport to the capillaries of adipose tissue and skeletal muscle (Figure 1). Here they are exposed to the lipoprotein lipase and release fatty acids and monoglycerides, which are transported into fat and muscle tissue. These fatty acids are then oxidized or re-esterified to become triglycerides. The triglyceride-depleted

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and cholesteryester-, apoprotein-B48-, and E-rich chylomicrons, which are now called *chylomicron remnants*, are taken up by the liver via specific chylomicron remnant receptors. In this way triglyceride has been brought to the fat depots and cholesterol to the liver. Cholesterol is transformed partly to bile acid, partly excreted unchanged in the bile, and partly distributed to extrahepatic tissue.

Carbohydrates from food are transformed to fatty acids in the liver, where they are esterified with glycerol to form triglycerides. Triglycerides are incorporated into VLDL and secreted into the blood. VLDL-triglycerides containing apoprotein-B100, -CII, and -E are hydrolyzed by the lipoprotein lipase and changed to VLDL remnants or intermediate-density lipoprotein (IDL). Because the LDL receptor recognizes both apoprotein-B-100 and -E, a portion of the IDL particles which contains both B100 and E is bound to LDL receptors in the liver and catabolized (the shunt pathway). The remaining IDLs remain in plasma and are further depleted for triglycerides and changed to cholesterol- and apoprotein-B100-rich LDL. Sixty to 80% of LDLs are normally removed from the liver but the rest are removed by extrahepatic tissue. One of the functions of LDLs is to transport cholesterol to peripheral tissue (adrenal cortex, lymphocytes, muscle and kidney cells), which also have LDL receptors. The liberated cholesterol is used for, among other things, the synthesis of membranes and as steroid hormone precursor. Nonesterified cholesterol that is released from peripheral cells is bound to HDL where it is coupled to fatty acids catabolized by lecithin-cholesterol acyltransferase (LCAT). The cholesteryl esters on the surface of HDL are transferred to VLDLs and eventually end up in LDLs. In this way a cycle has been established in which LDLs deliver cholesterol to

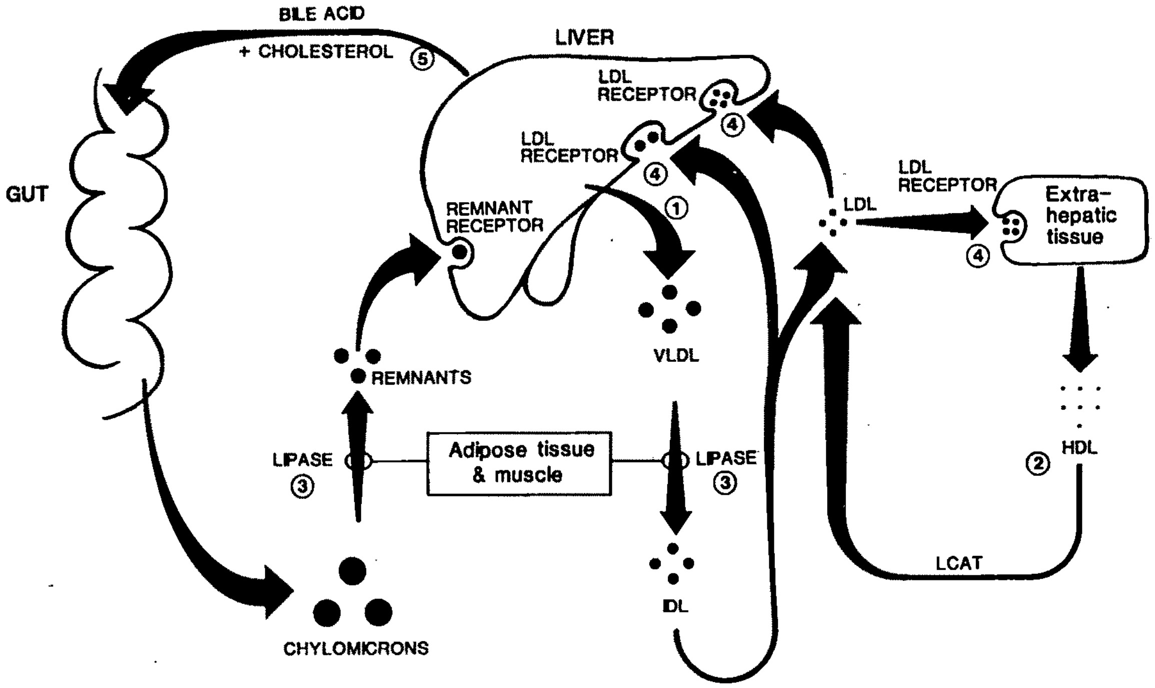

FIGURE 1. Lipid transport and probable site of action of the most common lipid-lowering drugs. 1. Decrease low-density lipoprotein (LDL) synthesis: nicotinic acid and fibrates. 2. Increase high-density lipoprotein (HDL) synthesis: nicotinic acid and fibrates. 3. Stimulate lipoprotein lipase activity: fibrates. 4. Increase LDL-receptor number: bile acid sequestrants, hepatic hydroxymethylglutaryl coenzyme A reductase inhibitors, probucol? 5. Increase fecal bile acid excretion: bile acid sequestrants, probucol. (IDL = intermediate-density lipoproteins; VLDL = very-low-density lipoproteins; LCAT = lecithin-cholesterol acyltransferase.)

extrahepatic tissue and cholesterol is then returned from extrahepatic tissue via HDLs. Cholesterol in the blood originates partly from food and partly from de novo synthesis of cholesterol. 3-Hydroxy-3-methyglutaryl-coenzyme A (HMG-CoA) reductase is a rate-limiting enzyme in the cholesterol synthesis.

Diabetes and Hyperlipidemia

One of insulin's many functions is to coordinate the conversion of carbohydrate in food to stored energy (triglycerides) in fat.[7] VLDL and chylomicrons, which transport endogenous and exogenous triglycerides, are broken down by lipoprotein lipases. In insulin deficiency, the activity of the lipoprotein lipases is decreased,[8] and this is one of the most common causes of hyperlipidemia in poorly controlled diabetes.[9] Investigations in diabetic animals seem to indicate that the production of VLDL-triglycerides in the gut is also controlled by insulin because insulin-deficient animals have increased production from the gut of VLDL-triglycerides.[10-12]

The hepatic triglyceride lipase is also insulin sensitive and is therefore also of importance for the lipoprotein abnormalities in diabetes mellitus.[13] During the action of lipoprotein lipases in fat tissue, the chylomicrons and VLDLs lose their triglycerides. These so-called chylomicron and VLDL remnants contain apoprotein E, which is mainly responsible for the LDL-receptor-mediated uptake by the liver. It is still not known how insulin influences the receptor's activity.

It also still has not been determined whether insulin stimulates the VLDL triglyceride secretion from the liver directly. The most plausible explanation is based on the premise that the elevated plasma nonesterified fatty acid (NEFA) concentration, even at normal insulin levels, results in an increased hepatic VLDL-triglyceride secretion concomitant with elevated plasma triglyceride concentrations.[14] The esterified cholesterol that appears in cholesterol-rich lipoproteins LDL and IDL (i.e., VLDL remnants) arises from free cholesterol uptake by HDL from peripheral cells followed by esterification through LCAT. This peripheral cholesterol removal may be impaired by the lack of insulin.[15] Investigations done on human skin fibroblasts seem to indicate that LDL receptor activity is increased by insulin.[16]

It should also be mentioned that insulin helps to balance the apoprotein composition of lipoproteins involved in enzymatic activation (e.g., apoprotein A1/A2 and apoprotein C2/C3 ratio) and receptor-mediated uptake of lipoproteins (apoprotein B and E contents).[17,18]

Changes in Plasma Lipoprotein Concentration in Patients with Insulin-Dependent Diabetes Mellitus

Insulin-dependent diabetes mellitus (IDDM) is characterized by absolute insulin deficiency. The deficiency results in hyperglycemia and eventually ketoacidosis and pronounced hypertriglyceridemia mainly because of insufficient activation of the lipoprotein lipase system.[19] Elimination of VLDL and chylomicrons is decreased, and especially in ketoacidosis, there is a marked increase in triglyceride-rich lipoproteins. An excess NEFA concentration resulting from increased lipolysis in fat tissue in insulin-deficient diabetes contributes to the increased hepatic triglyceride synthesis and secretion. VLDL, LDL, and HDL triglyceride contents are all increased in poorly controlled IDDM. An elevated triglyceride content in VLDL and LDL is due to the accumulation of triglycerides in these particles, but the cause of the elevated HDL triglyceride content is the result of an exchange of cholesteryl esters for triglycerides that takes place among HDLs, VLDLs, and LDLs. Insulin deficiency causes an increase in the LDL-cholesterol concentration because of decreased receptor binding, and also partly as a consequence of nonenzymatic glycation of LDL and partly because of an increased cholesterol/apoprotein B ratio in LDL in IDDM.

In patients with well-controlled IDDM, the total cholesterol, total triglycerides, and LDL-cholesterol concentrations do not differ from those of non-diabetic controls.[20] IDDM patients with coronary heart disease do, however, have significantly higher levels of total triglyceride, LDL-cholesterol, and VLDL-triglyceride and lower levels of HDL-cholesterol than do IDDM patients who do not have coronary artery disease.[21] The changes in the lipoprotein composition in patients with IDDM are thus dependent on the degree of glycemic control.

In conclusion, in poorly controlled diabetes, VLDL, LDL, and HDL become triglyceride-rich and there is an overproduction of VLDL and LDL and decreased removal of VLDL remnants. There is a decreased cholesterol/apoprotein B ratio in LDLs and the receptor binding of these changed LDL particles is decreased. In patients with well-controlled IDDM, the single alteration may be a slightly elevated HDL-cholesterol level due to high concentration of peripheral insulin, causing high lipoprotein lipase activity.

Changes in Plasma Lipoprotein Concentration in Patients with Non-Insulin-Dependent Diabetes Mellitus

Patients with non-insulin-dependent diabetes mellitus (NIDDM) have a high insulin concentration in the portal vein. This hepatic hyperinsulinemia leads to overproduction of VLDLs and triglycerides, but the relative insulin deficiency due to insulin resistance in the periphery results in decreased catabolism of triglyceride-rich lipoprotein because of decreased lipoprotein lipase activity[22] and to an increase in the concentration of NEFA because of increased lipase activity in the fat cells. It is also possible that the particle composition of VLDL is altered as well. Increases in the proportions of apoproteins C and E compared to other components of VLDL in NIDDM have been demonstrated that could lead to inhibited or delayed uptake in the liver. Generally, nearly normal LDL levels have been shown in NIDDM despite a decreased fractional catabolic rate of apoprotein B in LDLs. Large and triglyceride-rich VLDL particles especially exist in marked hyperglycemia, but the conversion to LDL is diminished. This may explain why LDL concentrations are normal or even reduced in NIDDM patients. The alterations in lipid composition and the glycation of LDL are the main causes of decreased receptor binding in NIDDM.[23]

The causes of the low HDL cholesterol levels in patients with NIDDM are yet undiscovered.[22,24] This decreased level of HDL may be indicative of an atherogenic factor but may also be the result of a demonstrated increase in hepatic lipase activity (antiatherogenic action).

There is no doubt that poorly controlled diabetes in patients with both IDDM and NIDDM is associated with atherogenic lipoprotein profiles in the blood. The management of the diabetes should therefore aim at regulating the blood glucose level as well as lipid concentrations. Whether the peripheral hyperinsulinism, which certainly persists for many hours per day in well-controlled patients, contributes additionally to the pathogenesis of atherosclerosis is as yet an unsettled question.[25] A review of the lipoprotein changes in diabetes mellitus has recently been published.[26]

Diagnosis of Hyperlipidemias in Diabetes

An accurate diagnosis of lipid disorders is essential to establish appropriate therapy (Figure 2). Various factors influence the serum concentration of lipids and lipoproteins, thus the measurement should be made under well-controlled conditions. Patients should be on a regular diet, not on medication that could affect lipid metabolism, have stable weight, and should not be, or have

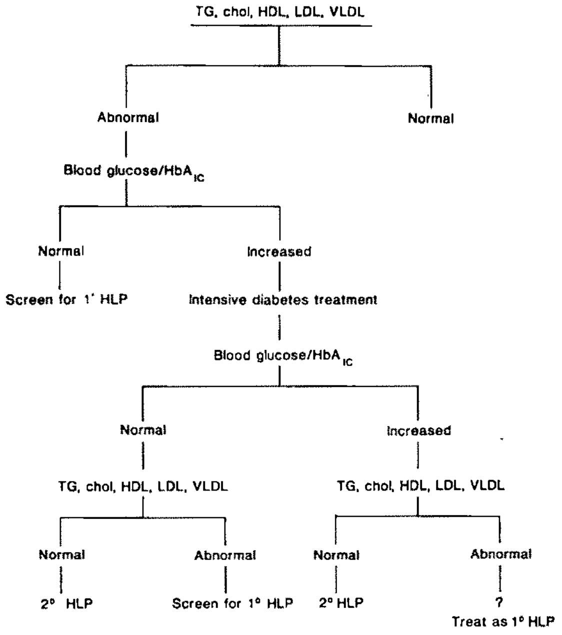

FIGURE 2. The diagnostic decision process in lipid disorders in diabetes mellitus. (Adapted from reference 33.) (TG = triglycerides; HDL = high-density lipoprotein; LDL = low-density lipoprotein; VLDL = very-low-density lipoprotein; HLP = hyperlipoproteinemia.)

TABLE 1. *Types of lipid/lipoprotein disorders in diabetes mellitus.*

Lipid disorder	Lipoprotein abnormality
Chylomicronemia syndrome	Raised VLDL and chylo; lowered HDL
Endogenous hypertriglyceridemia	Raised VLDL; lowered HDL
Combined hyperlipidemia	Raised VLDL and LDL
Dysbetalipoproteinemia	Raised chylo and VLDL-remnants
Hypercholesterolemia	Raised LDL
Hypoalphalipoproteinemia	Lowered HDL

VLDL = very-low-density lipoprotein; Chylo = chylomicron; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

recently been, acutely ill. Diagnosis should include a comprehensive personal and family history and a complete physical examination that assesses for arcus cornea, eruptive cutaneous and tendinous xanthomas, xanthelasma, lipemia retinalis, and premature atherosclerosis. Plasma cholesterol, triglycerides, and HDL-cholesterol levels should be measured after a 12- to 14-hour overnight fast. This requirement is mainly related to the measurement of triglycerides since triglyceride concentrations vary widely throughout the day depending on food intake. It is necessary to exclude all forms of secondary hyperlipidemia, especially hypothyroidism, nephrosis, and renal insufficiency. The classification of the lipid/lipoprotein disorders in diabetes mellitus is based on the fraction of lipids that are altered, as shown in Table 1. Endogenous hypertriglyceridemia and combined hyperlipidemia are each seen in about one fourth, hypercholesterolemia in about one fifth, and chylomicronemia syndrome in about one sixth of diabetic patients with hyperlipidemia.

Treatment of Hyperlipidemias in Diabetics with Drugs

The results of the Lipid Research Clinic investigation[27] showed unequivocally that lowering of the high LDL-cholesterol concentration leads to a decreased incidence of coronary artery disease. This finding was further supported by a study that showed a significant reduced mortality in patients with heart disease treated with nicotinic acid (niacin).[28] Elevated plasma lipid levels may be found in 25 to 50% of diabetic patients.[29] There are two main objects to reducing plasma lipid levels, both in diabetic and nondiabetic subjects, namely to avoid the occurrence of acute abdominal pain and pancreatitis because of severe hypertriglyceridemia, and to try to prevent, stop, or reverse atherosclerosis.

Therapy for diabetic patients aims at the normalization of lipid and lipoprotein levels, the establishment of adequate glucose hemostasis, and the prevention or treatment of other factors that may contribute to acceleration of atherosclerosis or to pancreatitis. To attain the first goal, the normal level for lipid and lipoprotein must be precisely defined (Table 2). A LDL/HDL ratio of more than 4 or a total-cholesterol/HDL ratio of more than 4.5 is considered atherogenic. When the total triglyceride level is below 5 mmol/L, LDL-cholesterol can be calculated from the Friedewald equation: LDL = total cholesterol − (HDL-cholesterol + triglycerides/2.19).

The initial treatment is dietary management for at least three months before drug therapy is started. The principle of diet management of hyperlipidemia is out of the scope of this paper and will not be discussed. In the case of familial

TABLE 2. *Guidelines for lipid and lipoprotein levels.*

NIH Consensus*	
Cholesterol	
Under 30 years of age	< 4.6 mmol/L
Over 40 years of age	< 5.3 mmol/L
Study Group of the European Atherosclerosis Society†	
Cholesterol	< 5.2 mmol/L
Triglyceride	< 2.3 mmol/L
High-density lipoprotein	> 0.9 mmol/L

*National Institutes of Health Consensus Conference. Lowering blood cholesterol to prevent heart disease. JAMA 1985; 253:2080-6.

†Study group of the European Atherosclerosis Society. Strategies for the prevention of coronary heart disease: A policy statement of the European Atherosclerosis Society. Eur Heart J 1987;8:77-88.

hypercholesterolemia with a cholesterol concentration over 10.4 mmol/L, the drug treatment can be started at the same time as the diet. Because dyslipoproteinemia responds well to pharmacological therapy and most cases will require drug therapy, drug and diet treatment may be initiated simultaneously. The flow chart in Figure 3 shows the decision process to follow in establishing drug therapy.

Table 3 lists the lipid-lowering drugs and their method of action. Table 4 shows the first and second choices in pharmacological therapy. For further description of the different drugs, pharmacology, and dosages, pharmacological textbooks should be consulted.

In cases of severe hypolipidemia, it is often necessary to combine hypolipidemic drugs. Almost all first-choice drugs (Table 4) can be combined. The combination of cholestyramine or cholestipol with niacin is very effective in lowering LDL-cholesterol. The combination of niacin and fibrate is useful in the event of severe hypertriglyceridemia. Probucol or fibrates are used together in the treatment of mild combined hyperlipidemia. The usual first choice of drug for the treatment of hypercholesterolemia is not always ideal for diabetics, however. Bile acid sequestrants can accentuate hypertriglyceridemia and niacin can decrease the glucose tolerance. HMG CoA reductase inhibitors decrease cholesterol synthesis and increase LDL receptor synthesis in the liver, resulting in increased removal of LDL-cholesterol and VLDL remnants from the circulation and in a significant decrease (compared with placebo) in total cholesterol (26%), LDL-cholesterol (28%), triglyceride (31%), and VLDL-triglyceride (42%) concentrations in the blood of patients with NIDDM and mild to moderate hypercholesterolemia. No change in the HDL-cholesterol concentration is noticed in these patients.[30] Bezafibrate is perhaps an even more ideal drug for diabetics with hyperlipoproteinemia because, in addition to increasing the HDL-cholesterol content (15%) and lowering the total

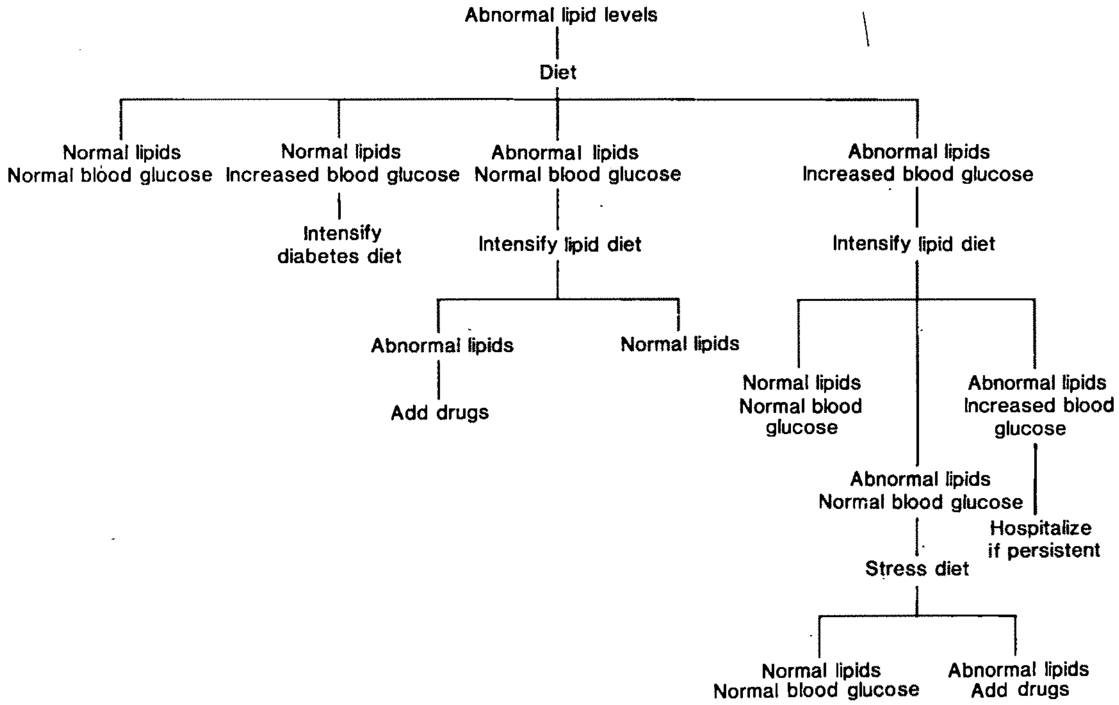

FIGURE 3. Flow chart showing the decision process for determining therapy in lipid disorders in diabetes mellitus. (Adapted from reference 33.)

cholesterol (17%) and triglyceride (36%) levels, bezafibrate also lowers fasting blood glucose (1 mmol/L) (31%) and glycated hemoglobin (hemoglobin A_1).[31,32]

Diuretics increase triglyceride and LDL-cholesterol concentrations and lower HDL-cholesterol levels. The alpha blocker prazosin increases the concentration of HDL. The angiotensin converting enzyme inhibitor captopril does not have any atherogenic effect on the lipid metabolism. Enzyme inductors such as barbiturates, phenytoin, and alcohol tend to increase the HDL-cholesterol concentration. Two review papers on the pharmacological treatment of lipid disturbances in diabetes mellitus have recently been published.[33,34]

Conclusion

The first step in the treatment of hyperlipidemia in diabetics is control of blood glucose. Dietary control of both hyperglycemia and hyperlipidemia

TABLE 3. *Effects of hypolipidemic drugs on lipids and lipoproteins.*

	Effects	Results
Inhibitors of bile acid absorption:		
Cholestyramine, colestipol, neomycin	Increase fecal bile acid excretion, increase LDL-receptor synthesis, inhibits cholesterol absorption from gut	Decreased cholesterol, increasing LDL-receptors
Antilipolytics:		
Niacin (nicotinic acid)	Inhibits lipolysis in fat tissue	Decreased cholesterol, triglycerides, and VLDL; increased HDL
Fibrates:		
Clofibrate, bezafibrate, gemfibrozil, fenofibrate, ciprofibrate	Increase lipoprotein lipase activity, inhibit HMG-CoA reductase (?)	Decreased triglycerides and VLDL
Probucol	Increase fecal bile acid excretion, inhibit hepatic cholesterol synthesis and apoprotein B synthesis	Decreased LDL-cholesterol and VLDL
HMG-CoA reductase inhibitors:		
Mevastatin, lovastatin, simvastin	Inhibit cholesterol synthesis in liver, increase LDL-receptor synthesis	Decreased LDL-cholesterol and VLDL

LDL = low-density lipoproteins; VLDL = very-low-density lipoproteins; HDL = high-density lipoproteins; HMG-CoA = 3-hydroxy-3-methylglutanyl-coenzyme A.

TABLE 4. *Drugs used in the treatment of lipid/lipoprotein disorders in diabetes mellitus.*

	Pharmacologic therapy	
Lipid disorder	1st choice	2nd choice
Chylomicronemia syndrome	Gemfibrozil	Niacin, clofibrate bezafibrate
Endogenous hypertriglyceridemia	Gemfibrozil	Niacin, clofibrate bezafibrate
Combined hyperlipidemia	HMG-CoA reductase inhibitors, niacin, gemfibrozil, colestipol, cholestyramine	Probucol
Dysbetalipoproteinemia	HMG-CoA reductase inhibitors, clofibrate, bezafibrate	Gemfibrozil, niacin
Hypercholesterolemia	HMG-CoA reductase inhibitors, colestipol, cholestyramine, niacin	Probucol

HMG-CoA = 3-hydroxy-3-methylglutaryl-coenzyme A.

should precede the treatment using antidiabetic and hypolipidemic drugs. Weight loss, exercise, and avoidance of excessive alcohol intake, as well as discontinuation of drugs known to increase the plasma lipid concentration, are necessary. Hypolipidemic drugs should only be used when satisfactory results are not obtained through optimal diet. Optimal treatment with antidiabetic agents precedes treatment with hypolipidemic drugs.

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Case Reports

DISTALGESIC (DEXTROPROPOXYPHENE) ADDICTION IN YEMENI PATIENT

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Distalgesic tablet is a proprietary preparation containing 32.5 mg of dextropropoxyphene hydrochloride B.P. (equivalent to approximately 30 mg dextropropoxyphene base) with 325 mg of paracetamol. The tablets are white, pillow-shaped, film-coated, 14 mm in length, and marked "DG." It is also available in a soluble tablet containing 50 mg of dextropropoxyphene napsylate B.P. (equivalent to 32.5 mg of dextropropoxyphene hydrochloride or 30 mg of dextropropoxyphene base) and 325 mg of paracetamol. The tablets are white and octagonal, with a diameter of 12.5 mm and marked "DGS." It is available in the Middle East and is easy to get in the Yemen Arab Republic. It is widely prescribed for mild or severe pain, either alone or with other drugs.

Both components are effective analgesics when given by mouth. Dextropropoxyphene was introduced as a substitute for codeine in 1957 and was claimed to be nonaddictive, but dependence has been widely reported in the United States as well as from Britain.[1]

I describe a case of distalgesic addiction in a Yemeni patient. I believe this is the first report of distalgesic addiction from the Arabian peninsula and the Middle East.

Case Report

A 38-year-old Yemeni man began taking distalgesic two years before for low back pain due to a lumbar disc lesion. After several months of uninterrupted use, he developed tolerance to its effect. He gradually increased his dose to 20 tablets daily over the next 18 months to achieve the drug's original effect. He denied any history of alcohol intake and no history of other drug abuse (e.g., tranquilizers, sedatives, or hypnotics).

While taking the drug he felt well, confident, and able to face the stresses of life. However, when he did not take the drug, withdrawal symptoms resulted, in the form of yawning, lacrimation, rhinorrhea, sweating and shivering, nausea, headache, and disturbed sleep or insomnia. He also became bad tempered, irritable, and depressed. All these symptoms would peak within 36 to 72 hours after the last dose and would subside on taking the drug, thus he had a severe craving for it. He was therefore admitted to the hospital for observation, investigation, and withdrawal therapy.

Hematological findings were normal, apart from a raised mean corpuscular volume of 104 fL (reference interval, 84-99). Total bilirubin was 38.3 μmol/L (reference interval, 2-18), and gamma-glutamyltransferase activity was increased at 0.83 μkat/L (reference interval, 0-0.50). Renal and hepatic functions had been normal prior to distalgesic abuse. A liver biopsy performed after admission showed zonal necrosis and sinusoidal congestion, and these were related to paracetamol hepatotoxicity, especially the patient's taking more than 4 gm per day for such a long time. Treatment consisted of withdrawal of the drug and methadone therapy, with tapered doses starting with 5 mg four times daily and decreasing the daily dose by 5 mg every third day. He was discharged home after two weeks and was taking no drugs at that time. He had felt well while on methadone and experienced no withdrawal symptoms. He was seen twice as an outpatient with low-grade withdrawal symptoms consisting of slight tremulousness, insomnia, and headache. On the third visit, six weeks after discharge, his symptoms were continuing to abate and he had not resumed taking the distalgesic.

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Discussion

Dextropropoxyphene is the psychoactive component of the distalgesic tablets which are widely used in the Middle East. It is frequently substituted for Aspirin in home medicine cupboards. Dextropropoxyphene is an analgesic related to methadone, and is mainly used in conjunction with other analgesics such as Aspirin or paracetamol that possess antiinflammatory and antipyretic effects. It is rapidly absorbed from the gastrointestinal tract and passes readily from the blood into body tissues. Dependence on dextropropoxyphene is of the morphine type, but it is claimed to be nonaddictive with no withdrawal signs. The first report of dextropropoxyphene dependence was published in 1960 by Fraser and Isabell and described five affected patients. In 1963 Elson and Domino[2] reported a case of dextropropoxyphene dependence in a 28-year-old man who consumed daily doses of 960 mg. Further reports of dependence followed.

Our patient took twenty 30-mg tablets daily, for a total daily consumption of 600 mg, though doses of less than 750 to 800 mg are claimed not to produce severe withdrawal symptoms. Concern has also increased regarding the dangers of dextropropoxyphene as a cause of death following acute overdosage, especially when taken with alcohol or other centrally acting drugs.[3]

Successful treatment of dextropropoxyphene dependence with methadone on a tapering scale over 10 days was reported in a 41-year-old woman who had a history of multiple drug abuse.[4]

Controlled studies have shown that dextropropoxyphene is not more efficacious than paracetamol or Aspirin alone,[5] though it is less potent than codeine (65 mg of dextropropoxyphene is equivalent to 30 to 45 mg of codeine). This study concluded that the combination of dextropropoxyphene and paracetamol has few advantages and a number of disadvantages over paracetamol alone.[5] With addiction an additional hazard of dextropropoxyphene use, the continued widespread use of the agent should be discouraged, especially since dextropropoxyphene is not considered superior to alternative safer analgesics.[6]

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PARADOXICAL RESPONSE OF INTRACRANIAL TUBERCULOMA DURING TREATMENT

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Chemotherapy is effective in the management of pulmonary and extrapulmonary tuberculosis, but patient tolerance and compliance to treatment as well as the susceptibility of the microorganism determine the success of treatment. In some patients, however, there is an unusual expansion or new formation of tuberculous lesions during treatment, and this reaction has been referred to as a "paradoxical response."[1] Although tuberculosis is common in Saudi Arabia,[2] such incidents do not appear to have been reported. We describe a patient with miliary tuberculosis who reacted paradoxically to chemotherapy.

Case Report

A 70-year-old Saudi man presented at King Khalid University Hospital because of cough with sputum, shortness of breath, headache, and bodyache. His temperature was 36.5°C; pulse, 89/min; respiratory rate, 21/min; blood pressure, 110/80; and weight, 50 kg. On examination the patient was found to be emaciated with evidence of weight loss. Cervical and axillary lymphadenopathy were found. There were a few basal crepitations of the right lung. The cardiovascular system was normal. Abdominal examination revealed an enlarged liver, especially the left lobe. Neurological examination revealed negative findings.

X-ray film of the chest showed miliary changes of the lungs. Sputum examination for acid-fast bacilli was negative. The clinical features and chest x-ray study were indicative of miliary tuberculosis, and the patient was treated with antituberculous drugs on an outpatient basis: rifampicin, 600 mg/day; isoniazid, 300 mg/day; pyrazinamide, 500 mg three times a day; ethambuatol, 600 mg/day; and pyridoxine, 40 mg per day.

There was subjective improvement in the patient's condition over the next 8 weeks of follow-up, but in the ninth week the patient was admitted to King Khalid University Hospital because of grand mal seizure. His temperature was 36.5°C; pulse, 80/min; and blood pressure, 120/80. The patient was conscious but disoriented to place and time. There was no lymphadenopathy, and chest, cardiovascular system, and abdominal findings were normal. Neurological examination was negative.

Laboratory investigations revealed the following findings: hemoglobin, 126 g/L, and erythrocyte sedimentation rate, 50 mm/h. Results of blood biochemistry and urinalysis were within normal limits and VDRL and Treponema pallidum hemagglutination (TPHA) were negative. Blood culture for *Brucella* was negative. Sputum examination for acid-fast bacilli was also negative. Chest x-ray study showed bilateral nodular shadowing that was more marked in the mid and upper zones (Figure 1). Computed tomogram (CT) of the brain revealed multiple small enhancing areas with surrounding edema (Figure 2) that was most probably due to multiple tuberculomas. Angiography was not done. Antituberculous drugs were continued, together with phenytoin (200 mg per day). Three weeks after admission, mild transient right-sided hemiparesis developed. Dexamethasone (4 mg intravenously every 5

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hours) was added and the dose was tapered slowly. After 5 weeks of hospitalization, the patient was discharged without neurological deficit. He was on antituberculous treatment.

Follow-up chest x-ray study showed disappearance of the miliary lung shadow after 5 months of continuous antituberculous treatment (Figures 3 and 4). Similarly, there was a substantial reduction in the masses seen on contrast-enhanced CT scan of the brain five months after the first seizure.

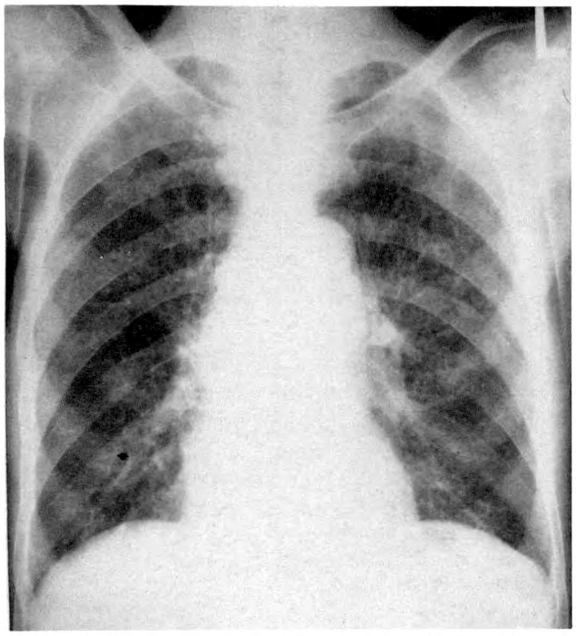

FIGURE 1. Plain chest x-ray study showing miliary mottling in both lung fields suggesting miliary tuberculosis (calcified right paratracheal lymph nodes).

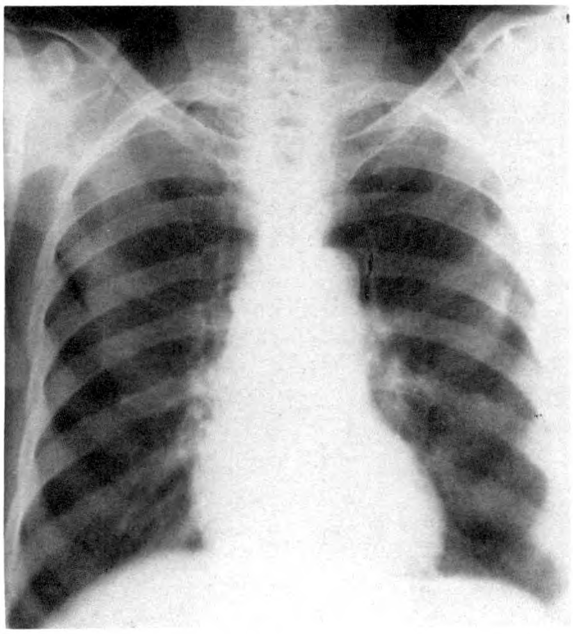

FIGURE 2. Follow-up chest x-ray study showing a clear lung field with no evidence of miliary shadowing.

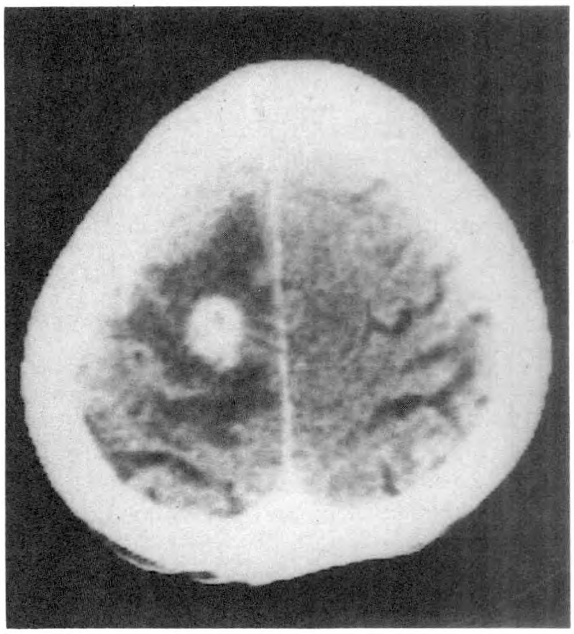

FIGURE 3. Post contrast computed tomographic brain scan showing an enhancing mass in the left parietal region with surrounding cerebral edema.

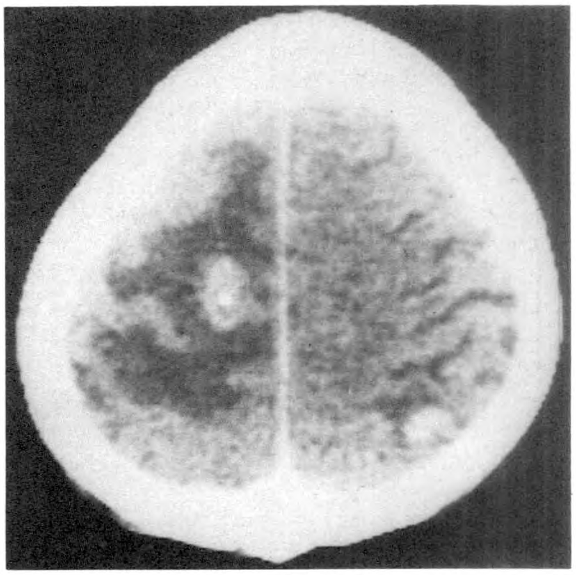

FIGURE 4. Post contrast computed tomographic brain scan done two weeks after the scan shown in Figure 3. There is significant reduction in the enhanced mass. Another small, new enhancing lesion in the right posterior parietal region can also be seen.

Discussion

Pulmonary miliary tuberculosis and tuberculous meningitis frequently co-exist, and CT scanning of the brain has shown the presence of tuberculoma in patients with tuberculous meningitis.[3] In patients with paradoxical response, intracranial lesions either developed or increased in size during chemotherapy.[3] Our patient presented with pulmonary miliary tuberculosis that was strongly suggested by the clinical course and changes on the chest x-ray film. The initial improvement with antitubercle chemotherapy supports the diagnosis of tuberculosis. The fact that neurological complications developed during his hospital stay, and his care supervised, makes poor compliance unlikely and favors a paradoxical response.

Paradoxical responses usually occur in three different tissues: lymph nodes, lungs, and brain. If patients with tuberculosis involving any of these organs worsen during treatment, a paradoxical response should be considered. The frequency of paradoxical responses is not known. Campbell and Dyson[4] found paradoxical enlargement in about 30% of their patients with lymph node tuberculosis. We reported paradoxical responses in a group of patients with tuberculosis of the cervical lymph nodes.[5] There are only a few reports of patients with intracranial tuberculomas that expanded during chemotherapy.[3] The explanation for this phenomenon is obscure, but it may be due to a hypersensitivity reaction to metabolic products during chemotherapy.

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PREPUBERTAL CATATONIC SCHIZOPHRENIA

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The syndrome of catatonia was first described by Karl Kahlbaum in 1874,[1] and included the symptoms of catalepsy, negativism, mutism, stereotypy, posturing, muscular rigidity, and verbigeration. Emil Kraepelin[2] regarded catatonia as a subtype of the dementia praecox he described, and Bleuler later called this disorder schizophrenia. Schizophrenia continued to be considered the main cause of catatonia, but since Gelenberg's 1976 paper,[3] there have been several reports that have emphasized the organic and affective etiology of catatonia and catatonia-like symptomatology.[4-6] The validity of catatonic schizophrenia has been increasingly questioned, with greater emphasis now placed on the nonschizophrenic aspect.

Though decreasing in incidence,[6] functional catatonia is relatively common in adults, but has been reported rarely in children. Bemporad and Dunton,[7] in a survey of the international literature, found only 22 cases of catatonia in childhood and noted that seizure disorders were related to the appearance of the catatonic episodes in many. They believed the catatonia in two of their patients was psychogenic and suggested an oppositional mechanism. Feinberg[8] reported the case of a 14-year-old girl with fever of unknown origin that was diagnosed as acute catatonic schizophrenia after a lengthy medical evaluation showed no organic mechanism. However, her disorder was complicated by sepsis, thrombocytopenia, convulsions, and abnormal electroencephalogram (EEG), with death occurring three months after admission, raising the possibility of a lethal form of catatonia.

Belfer and d'Autremont[9] described catatonia-like symptoms in a 16-year-old and attributed them to an arteriovenous malformation in the left frontal lobe. Shah and Kaplan[10] reported catatonic symptoms in a 10-year-old girl with abnormal EEG tracings who exhibited a dramatic response to intravenously administered phenytoin. They emphasized the organic etiology of catatonic symptoms in childhood. A case of steroid-induced catatonia was reported by Sullivan and Dickerman[11] in an 11-year-old boy with dermatomyositis.

Among 12 patients with catatonia secondary to typhoid fever reported by Breakey and Kala,[12] one was a 7-year-old boy who showed gradual improvement when treated with chlorpromazine.

Recently, five case reports have been published concerning adolescents with depressive stupor and other catatonic features followed by manic-like symptoms, suggesting the diagnosis of bipolar affective psychosis.[13-16] The conclusion was that catatonic signs in young adolescents should raise the suspicion of an underlying affective disorder rather than schizophrenia.

The case of an 11-year-old schizophrenic boy presenting with catatonia is reported. In a search of the recent literature, I failed to find a similar case. The case reported emphasizes the possible schizophrenic etiology of the disorder.

Case Report

An 11-year-old Muslim boy of bedouin background was admitted to the Paediatric Ward of King Khalid University Hospital (KKUH) in May 1986. He was stuperous, markedly emaciated (weight, 18 kg), and completely immobile with rigidity and flexed posture (Figure 1). He was also

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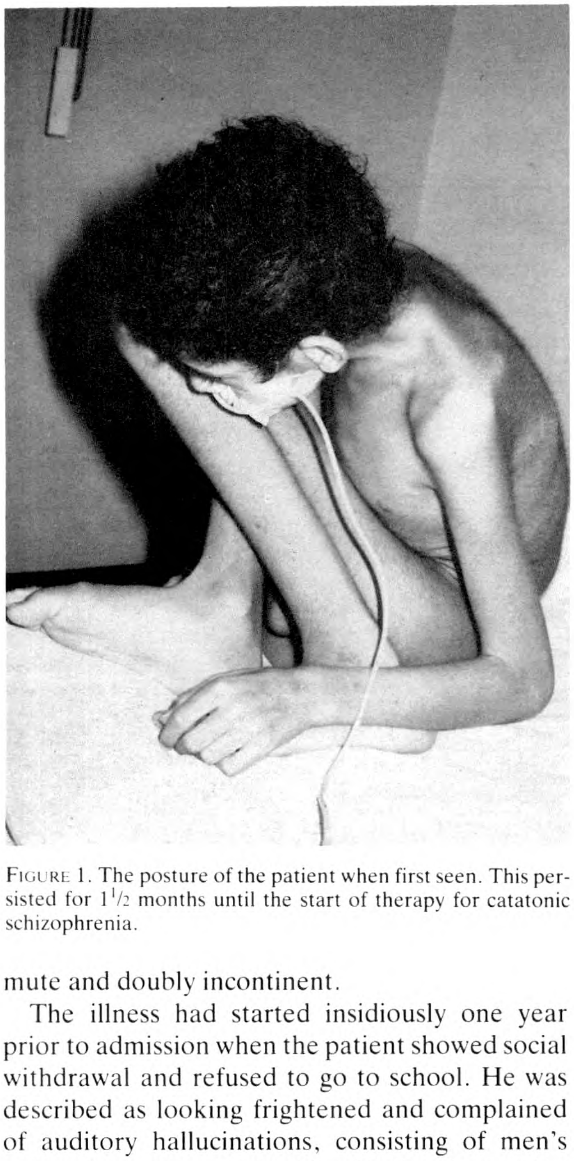

FIGURE 1. The posture of the patient when first seen. This persisted for $1^1/_2$ months until the start of therapy for catatonic schizophrenia.

mute and doubly incontinent.

The illness had started insidiously one year prior to admission when the patient showed social withdrawal and refused to go to school. He was described as looking frightened and complained of auditory hallucinations, consisting of men's voices threatening to stab him. During the ensuing weeks he slept less, lay motionless in bed whispering incoherently, and developed incontinence of urine and feces. On several occasions he stood motionless for hours and was unresponsive to his surroundings. He took inordinately long to dress and eat, and when asked a question he would repeat it over and over. By six months after the onset of the illness, he did not communicate verbally or nonverbally, almost totally refused food, had completely withdrawn, and was unable to take care of his basic needs. At this stage his family took him to traditional healers who prescribed herbs and recitation from the Holy Quran "to drive away the evil spirit (Jin) which inflicted the patient," but the patient's state remained unchanged until admission.

The patient came from a closeknit family of low socioeconomic status. His parents were first cousins. His mother was described as an introvert and was overprotective of the patient, who is the youngest of five siblings. A 25-year-old brother was reported to be "odd" following a head injury suffered in a car accident. A 22-year-old brother apparently had a "nervous breakdown" at the age of fifteen years and was leading a solitary life with no job and little family contact. Because the family were bedouin nomads, it was not possible to locate these two brothers for evaluation of a possible common underlying pathology shared with the patient described here.

The patient was the product of a normal pregnancy and delivery, with subsequent normal physical and mental development. He started school at 8, and did fairly well in the first and second grades, though he never enjoyed school and frequently complained of being bullied. He was described as a lonely child who had had few friends. His past medical history was unremarkable and there was no history suggestive of measles, rubella, chickenpox, or mumps. There was also no history of vaccination, trauma, ingestion of a toxic agent, or febrile or nonfebrile convulsions.

Medical and neurologic findings were normal, apart from symptoms of dehydration, gross emaciation, and axial and limb rigidity. He was afebrile; pulse was 120 per minute and blood pressure, 80/60.

Laboratory investigations included normal urinalysis, normal blood chemistry, and negative neurometabolic screening. The blood findings were normal apart from a hemoglobin of 9 g/L, with normal hemoglobin electrophoresis. Screening for collagen diseases, porphyria, and lead poisoning was negative. Hormonal assays for thyroid and parathyroid disorders were normal. The dexamethasone suppression test showed normal suppression. Serologic tests for viral antibodies using complement fixation tests against herpes simplex virus types I and II, chickenpox, mumps, poliomyelitis, and cytomegalovirus were negative. Antibodies against *Mycoplasma pneumoniae* were negative. Cerebrospinal fluid (CSF) showed normal opening pressure and composition. The CSF immunoglobulins were within normal ranges, and titers against the above-mentioned viruses were negative. Visual evoked responses, brainstem auditory evoked potentials, and EEG (including 24-hour EEG monitoring) were all normal. Chest x-ray studies were normal and two computed tomographic brain scans revealed no abnormality.

For the next four weeks his mental state did not change. He remained in a frozen fetal-like posture with total body rigidity and fragmented eye contact, but he continued to be alert (Figure 1). He remained mute, unresponsive, and negativistic with retention of saliva, urine incontinence, and preference for nudism. He crumbled all of his food and ate the particles, spending hours doing this. When asleep he was always curled up and sucked his thumb.

After a basically negative medical evaluation for an underlying organic cause, evidence of a functional psychiatric disorder was explored through an "amytal interview." Following intravenous administration of 100 mg of amytal sodium, the patient answered questions in monosyllables, revealing normal sensorium, and denied morbid depressive feelings but admitted to the auditory hallucinations described previously. His affect was that of fear and no delusions could be elicited. The patient became mute after about forty minutes.

A provisional diagnosis of catatonic schizophrenia was made and he was transferred to the KKUH Psychiatric Unit and started on trifluoperazine syrup (2 mg three times a day) via a nasogastric tube. A regimen involving a behavioral approach, milieu therapy, and physiotherapy was started. Six days later, he suffered an acute oculogyric crisis and the trifluoperazine was substituted with thioridazine, which was increased to a total daily dose of 300 mg. Over the next eight weeks, the patient showed gradual and slow improvement in almost all areas of functioning. His negativism and rigidity gradually abated and he became ambulatory, but his social and emotional interactions were limited. His speech was slowed and he showed poor eye contact with excessive blinking and fear. He regained full control of sphincters. His food intake became normal and his weight almost doubled to 35.2 kg (Figure 2). The auditory hallucinations ceased but he had full recollection of his illness. He was discharged in October 1986 on thioridazine maintenance therapy. During the $2^1/_2$ years of outpatient follow-up he has shown no signs of mania or depression, but there have been residual symptoms of emotional blunting, poor rapport, social withdrawal, and failure to regain his premorbid level of adaptive functioning.

Discussion

This case satisfied most of the DSM-III (Diagnostic and Statistical Manual, 3rd Edition) criteria for schizophrenia.[17] Clinically the patient exhibited a variety of catatonic features and regression in almost all areas of functioning, supporting the diagnosis of schizophrenia rather than a depressive stupor or an affective disorder. The patient's premorbid personality, age, and the insidious onset of the illness, which became chronic with emergence of negative symptoms and a lasting

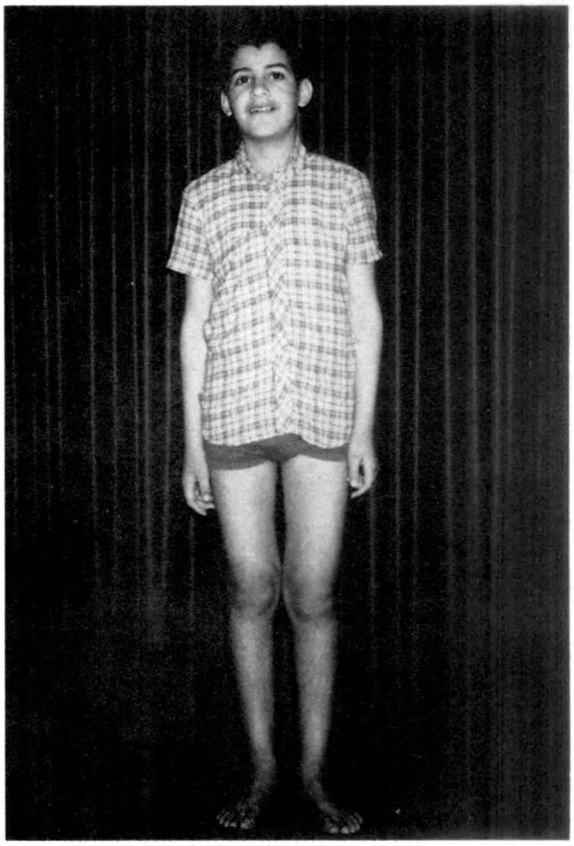

FIGURE 2. The patient following treatment for catatonic schizophrenia.

defeat, were suggestive of a schizophrenic illness rather than depressive stupor. The latter seemed unlikely because of the negative family history for an affective disorder, absence of mood change, and the normal dexamethasone suppression test.[15] The findings elicited during the "amytal interview" were more consistent with the diagnosis of schizophrenia. Furthermore, the response of the patient to phenothiazine with partial resolution of the psychosis and absence of subsequent manic episodes during follow-up seemed to favor this diagnosis.

The literature strongly supports the hypothesis that early onset schizophrenia is at the severest end of the schizophrenia spectrum.[18] This explains the poor outcome in our patient even though the type was catatonic. The early onset form carries a poor prognosis and this outweighs the good prognosis associated with the catatonic form.

An organic cause of catatonia should never be ruled out, especially when it occurs in patients from developing countries. However, the history and extensive medical evaluation in our patient produced essentially negative findings, suggesting a functional cause. The possibility of viral encephalitis also should not be ignored. Nunn et al[19] reported four cases of childhood psychosis associated with viral encephalitis, but all showed evidence of infection or neurodevelopmental abnormalities. There was no such association in our patient.

The symptoms of schizophrenia can be diverse and patients may present initially as a medical problem, as demonstrated by our patient.

In developing countries, the misconceptions concerning mental illness may delay early treatment, as occurred in our patient, and partly explaining the relative prevalence of catatonic disorders in such countries. Our case also demonstrates the continued need to consider a schizophrenic cause in the evaluation of patients with catatonia.

Acknowledgment

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FETAL SURVIVAL AFTER SUPPRESSION OF MATERNAL ANTICARDIOLIPIN ANTIBODY

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We report on fetal survival following treatment to suppress anticardiolipin in a patient who did not have systemic lupus erythematosus (SLE). Anticardiolipin antibody level was consistently reduced during treatment. Anticardiolipin antibody represents a specific group of antiphospholipid antibodies that essentially recognize cardiolipin. Its presence in pregnant women correlates highly with recurrent fetal loss, and its suppression with drugs like prednisolone and aspirin has permitted normal pregnancies and live births.[1-3]

Anticardiolipin antibody is found in association with various disorders, including SLE and thromboembolic hematological conditions.[4,5] The pathogenic role of anticardiolipin antibody is no longer disputed in that its presence in pregnant women seems to be related to fetal harm.[6]

Case Report

A 29-year-old Jordanian woman who had no living children was first seen prior to her fifth pregnancy. Her first pregnancy was terminated at 20 weeks because of toxemia. Her second, third, and fourth pregnancies resulted in intrauterine fetal deaths in the 24th, 8th, and 26th weeks, respectively. On each occasion, the placenta showed marked areas of infarct both on gross and histological examination. Complete obstetric and gynecological evaluation revealed no cause for her recurrent fetal losses.

History and physical examination for evidence of SLE was unrevealing, except that her erythrocyte sedimentation rate varied between 40 and 60 mm in the first hour. Serological tests revealed the following titers: VDRL, 1:4; antinuclear antibody, 1:40; deoxyribonucleic acid (DNA), 1:320. Her renal function and liver profile were normal. Clotting profile using prothrombin time, partial thromboplastin time, activated partial thromboplastin time, thrombin time, and fibrinogen levels, as well as platelet aggregation tests using adrenaline, collagen, arachidonic acid, and ristocetin, were all normal. Clotting profile was normal throughout her pregnancy. Anticardiolipin antibody levels were measured by radioimmunoassay and enzyme linked immunosorbent assay (ELISA) during the 8th week of her pregnancy. This was positive for IgG (102 μg/ml) and negative for IgM (MPL). The patient was started on 20 mg of prednisolone and 300 mg of aspirin daily beginning in the 14th week of pregnancy. She was evaluated frequently, both clinically and by ultrasound, and these confirmed normal fetal growth. By the 22nd week of pregnancy, the IgG cardiolipin antibodies had decreased to 24 μg/ml. In the 24th week, prednisolone dosage was reduced to 15 mg per day because of the development of mild hyperglycemia. The patient's IgG cardiolipin antibody level was 29 μg/ml during the 29th week.

A cesarean section was performed at 32 weeks, after consultation with the neonatologists, because of the patient's obstetric history and her considerable anxiety. A 2.1-kg, live and healthy female baby was delivered. The placenta was entirely free of infarcts. IgG cardiolipin anti-

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bodies in a concentration of 10 μg/ml were detected in the fetal umbilical cord blood. No neonatal complications arose, and the baby is well and thriving two years later.

The patient had a second successful pregnancy a year later, which resulted in a 2.2-kg, healthy male infant who is alive and well.[4] The patient has since delivered a third live baby at 34 weeks' gestation, weighing 930 grams. This infant is doing well in the neonatal intensive care unit at the time of this report. All three successful pregnancies were achieved following immunosuppression treatment.

Initial testing of anticardiolipin antibody by solid-phase radioimmunoassay was performed at St. Thomas Hospital, London.[5] It was later tested by ELISA and confirmed by us after proper standardization against five test samples provided by the Lupus Research Laboratory, London, covering a wide range of anticardiolipin antibody values, both IgG and IgM, local controls, and test standards provided by Cheshire Diagnostics Laboratory, England.[7] The coefficient of variation ranged from 0.99 for IgM to 0.98 for IgG, using a Virgo ELISA reader (Electro-nucleonics). Comparisons were made by regression lines plotted by the reader in logarithmic values of optical absorbance readings versus logarithmic values of the antibody test sample and controls. The degrees of positivity against the standards were assigned IgG and IgM units with definite cut-off points. Results were excellent and in line with observations of the Lupus Research Laboratory and other participating centers worldwide.

Discussion

Recurrent early pregnancy loss is a frustrating problem, both for the patient and physician. The presence of anticardiolipin antibody and lupus anticoagulant antibody correlates with fetal losses in patients with SLE and lupus-like disorders.[4,6] Studies have shown that anticardiolipin antibody, like lupus anticoagulant antibody, is strongly associated with both venous and arterial thrombosis.[8,9] Therefore the chance of successful pregnancy in a patient possessing these antibodies appears to be much less than that in the usual patients suffering recurrent abortions. It has been suggested that the two groups of antibodies, though closely related, constitute independent groups of antibodies that cover overlapping antigenic specificities directed against phospholipid.[7,10] The anticardiolipin antibody assay, unlike the lupus anticoagulant antibody assay, is more sensitive, has less observer error, and can be performed on stored sera.[11] Anticardiolipin antibody may appear several years before any clinical signs and indirectly cause lesions of the vascular endothelium through the action of complement-activating immune complexes or through recognition of phospholipid membrane antigen.[6] This process results in diminished parietal fibrinolytic activity, precipitating thrombosis and excessive release of von Willebrand's factor which is a potential source of hypercoagulability.[2,6] Anticardiolipin antibody determinations have proved useful in monitoring the treatment of women with recurrent fetal losses who show placental infarction and thrombosis. Its presence has been considered by some to be the most sensitive predictor of fetal loss.[12]

The demonstration of anticardiolipin antibody in our patient, its suppression, and the subsequent successful pregnancy after four unsuccessful pregnancies suggest that this antibody may be an underlying etiological factor in the placental infarcts. Early therapy has led to normal pregnancies in several reported cases.[3,11,13] Patients with lupus anticoagulant and anticardiolipin antibodies who have had previous unsuccessful pregnancy have gone on to deliver healthy infants following treatment with prednisolone (40-60 mg/day) and aspirin (75-80 mg/day), started as soon as pregnancy was detected.[12] Prednisolone usually suppresses the production or activity of lupus anticoagulant and cardiolipin antibody. Low-dose aspirin inhibits platelet aggregation and theoretically restores a normal thromboxane-prostacyclin balance.[12]

Although our patient had positive antinuclear antibody, deoxyribonucleic acid (DNA), and VDRL antibodies, these alone and in the absence of other features were inadequate to make a firm diagnosis of SLE.[14] This suggests that anticardiolipin antibody like lupus anticoagulant antibody may occur even in the absence of overt SLE. Our patient had a high titer of cardiolipin antibody but not lupus anticoagulant antibody. Conversely, Harris et al[5] found three of their 32 patients had lupus anticoagulant antibody in the absence of cardiolipin antibody, suggesting that these two assays do not estimate the same factor. We therefore feel that both factors should be sought when evaluating patients with recurrent fetal losses, and suppressed if found.

We have demonstrated that anticardiolipin antibody suppression by prednisolone plus aspirin improves the chances of fetal survival. We feel that regular cardiolipin antibody screening and suppression in pregnant women with recurrent abortions could lead to a high rate of fetal survival. Our observations agree with the experience of others.[1,3] However, we have reservations concerning the initiation of prednisolone and aspirin therapy during organogenesis, because of the potentially teratogenic effect of the two drugs. The therapy should be started soon after organogenesis, and when the timing of fetal loss has been ascertained.

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WERNER'S SYNDROME, PHEOCHROMOCYTOMA DUE TO AN ABDOMINAL PARAGANGLIONEUROMA, AND GEOPHAGIA IN AN ARAB

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Werner's syndrome was first described in 1904 by Otto Werner in his doctoral thesis, in which he reported four siblings with similar clinical findings, namely short stature, senile appearance, premature graying of the hair, early cataract formation, skin changes described as sclerodermatous, joint deformities, and atrophy of muscles and connective tissues of the extremities.[1] Werner's syndrome is a prototype of the so-called progeroid syndromes, i.e., disorders characterized by premature aging.

In their landmark review of the syndrome in 1966, Epstein et al[1] reported on 122 documented cases in the world literature and added three of their own from a single sibship. There has not been a comparable review since.

A computer search of the world literature did not turn up a single case that had occurred in an Arab. We report a case of Werner's syndrome in a Yemeni Arab who also had a pheochromocytoma due to an abdominal paraganglioneuroma and iron deficiency anemia secondary to geophagia (soil eating).

Case Report

A 41-year-old Yemeni man was admitted to King Khalid University Hospital, Riyadh, with a history of chest pain and dyspnea on exertion of six months' duration. He had also experienced poor vision for about one year and abdominal pain for several years. In addition, he had been known to exhibit geophagia for several years. He denied any episodes of palpitations, sweating, headache, postural dizziness, or syncope. His father and mother were first cousins. There was no family history of short stature or other similar problems.

On clinical examination, he was found to be a diminutive man (Figure 1) who had limited intelligence based on our subjective assessment. He looked at least 10 to 15 years older than his age, as

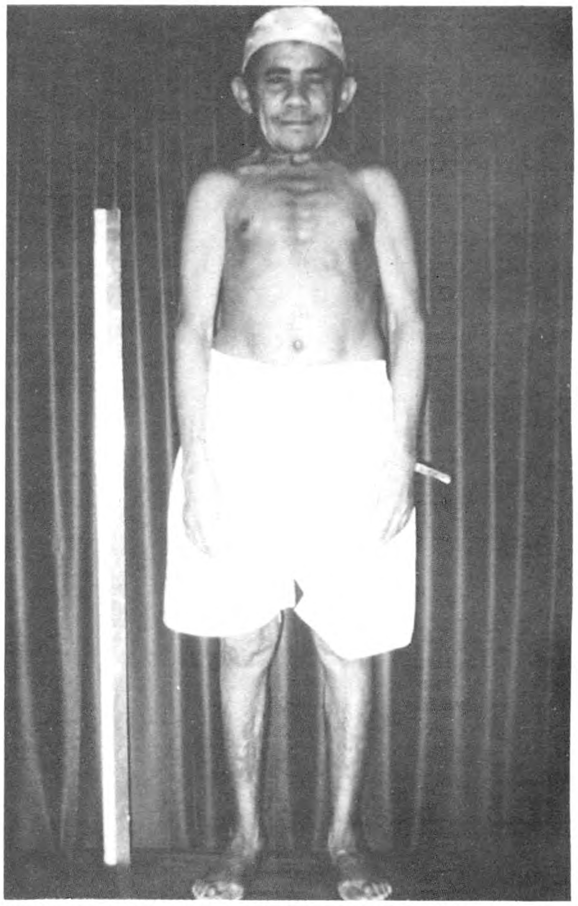

FIGURE 1. A 41-year-old Yemeni patient with Werner's syndrome. Note the short stature and the marked lining of the face.

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evidenced by crow's-feet around the eyes and wrinkles on his face. His height was 131.5 cm and weight was 32 kg. He looked very pale and had streaks of white hair and some hair loss in the frontal and temporal areas. He had bilateral cataracts and his facial hair was relatively scanty. He had no axillary hair and his pubic hair was very sparse with a female pattern distribution. His voice was thin, high pitched, and squeaky. Examination of his cardiovascular system revealed normal findings apart from an ejection systolic murmur at the mitral and aortic area. His blood pressure was 130/90.

Abdominal examination revealed a firm mass (12 × 8 cm) in the left lumbar region just lateral to the umbilicus. Examination of the central nervous system was normal, and he had an average sized penis and testes.

Initial Laboratory Data

His white blood cell count was 7.3 × 10^9/L; red blood cell count, 4.01 × 10^{12}/L; hemoglobin, 66 gm/L; hematocrit, 0.21; mean corpuscular volume, 52.3 fL; mean corpuscular hemoglobin concentration, 18.7 mmol/L; and reticulocyte count, 12 × 10^{10}/L. His serum iron was 4 μmol/L; total iron binding capacity, 98 μmol/L; and percent saturation 4.08. Routine admission biochemistry was normal and stool was negative for occult blood, ova, and parasites.

Electrocardiogram showed a sinus rhythm with left ventricular hypertrophy. The echocardiogram demonstrated hypertrophy of the left ventricular walls as well as thickened aortic valve and mitral annular calcification.

Chest x-ray study showed unfolding of the aorta and kyphoscoliosis of the thoracic spine. X-ray study of the feet, ankles, knees, and dorsal spine showed generalized osteoporotic changes. Abdominal ultrasound showed a mass on the left side of the abdomen which measured at least 12 × 7 × 5 cm. Computed tomographic (CT) scan of the abdomen (Figure 2) confirmed the presence of a large soft tissue mass anterior and to the left of the aorta. The left kidney was atrophic.

Initially the abdominal ultrasound and CT scan findings were interpreted as a gastrointestinal lesion, and the following procedures were done: colonoscopy, barium meal with follow-through, and a fine needle aspiration biopsy. During the aspiration biopsy, the patient's blood pressure was noted to rise sharply. Subsequently on the ward, a rise in the blood pressure from 130/90 to 230/130 was observed after abdominal palpation. Electron microscopic examination of cell block material obtained from fine needle aspiration demonstrated cells containing norepinephrine granules, and this was consistent with the diagnosis of a pheochromocytoma.

Figure 3 illustrates the findings from an iodine 131 metaiodobenzylguanidine scan.

Table 1 provides the results of hypothalamic pituitary function studies and the oral glucose

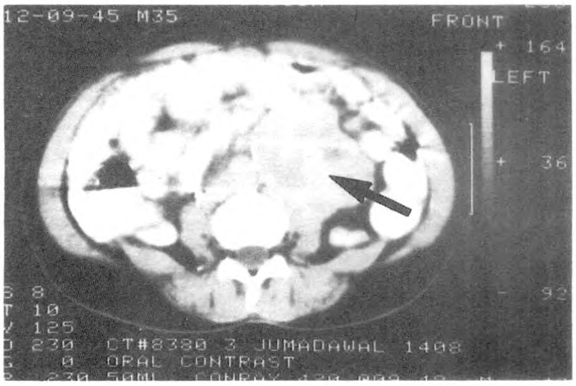

FIGURE 2. Abdominal computed tomographic scan showing a huge left paramedian mass (arrow).

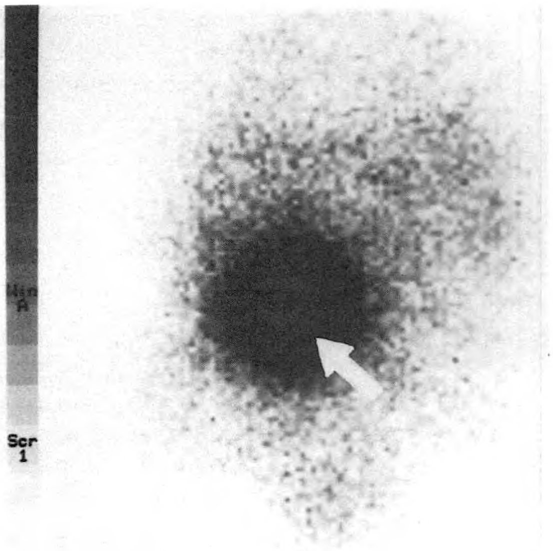

FIGURE 3. Scintigram (posterior view) taken after injection of I-131 metaiodobenzylguanidine, showing a functioning abdominal paraganglioneuroma.

tolerance test. These demonstrated an intact pituitary gland and normal carbohydrate tolerance with normal insulin responsiveness. Other hormonal data were as follows: urinary vanillylmandelic acid, 77 μmol/dL (reference interval, < 45); plasma norepinephrine, 33.6 nmol/L (reference interval, < 2.65); plasma epinephrine, 1.8 nmol/L (reference interval, < 0.68); plasma testosterone, 60.8 nmol/L (reference interval, 10.4 - 41.7); triiodothyronine (T_3), 1.9 nmol/L (reference interval, 0.8 - 2.46); and tetraiodothyronine (T_4), 61.8 nmol/L (reference interval, 542 - 142). The plasma zinc level was 6 μmol/L (reference interval, 11-20).

Hospital Course

The patient was treated with supplemental oral ferrous sulfate tablets for his anemia, and prior to surgical removal of the paraganglioneuroma, the patient was transfused with two units of packed cells. Following initial alpha-adrenergic receptor blockade with phenoxybenzamine (Dibenzyline) for anesthesia, the paraganglioneuroma was surgically excised uneventfully. The atrophic left kidney was also removed. The histopathology report on the tumor confirmed that it was a pheochromocytoma. Postoperatively the patient's blood pressure ranged between 110/80 to 130/80.

Discussion

In a review of disorders of accelerated aging, Martin[2] indicated that Werner's syndrome belongs to the progeroid syndromes and these have been classified into two categories. Segmental progeroid syndromes, of which Werner's and Down's syndromes are examples, involve multiple aspects of the senescent phenotype. Unimodal progeroid syndromes involve predominantly one aspect of the phenotype and examples include xeroderma pigmentosum and hypercholesterolemia (accelerated atherogenesis).

Thannhauser[3] has listed 12 principal characteristics of Werner's syndrome, but even the classic review by Epstein et al[1] did not specify the minimum criteria for diagnosis. However, Werner was quoted as being impressed principally by the cataract formation, skin changes, senile appearance, and graying of the hair.[1] Our patient had a profoundly short stature and small body size, premature graying of his hair, a facial appearance older than his chronologic age, bilateral cataracts, a thin high-pitched voice, thin extremities with hyperkeratosis of both feet, absent axillary hair with a female type distribution of pubic hair, and widespread osteoporosis. In addition, his parents were first cousins, which conforms to the autosomal recessive pattern of inheritance described for the disease.

There has not been any clear explanation of the various features of Werner's syndrome. Epstein et al[1] examined several aspects of the syndrome, and in particular the endocrine status. They concluded that there was no specific hormonal deficiency or

TABLE 1. *Pituitary dynamic function studies* and oral glucose tolerance test.†*

	Time					
Hormone	0	20	30	60	90	120
Cortisol (nmol/L)	389.0	435.9	606.98	612.5	612.5	695.2
GH (mU/L)	1.8	2.9	6.2	8.1	13.9	20.6
LH (IU/L)	19.9	130		168		
FSH (IU/L)	12.9	22.9		31.1		
TSH (mU/L)	1.7	15.9		12.2		
Prolactin (mIU/L)	247.7	1468.8		2208		
OGTT						
Glucose (mmol/L)	3.4		5.4	8.0	8.3	6.6
Insulin (pmol/L)	32		158	314	338	212

*Intravenous cocktail comprising 200 μg of thyrotropin releasing hormone, 100 μg of gonadotropin releasing hormone, and 0.1 μ/kg body weight of insulin administered after baseline blood.

†Oral glucose load = 75 g.

TSH = thyroid stimulating hormone; GH = growth hormone; LH = luteinizing hormone; FSH = follicle stimulating hormone; OGTT = oral glucose tolerance test.

excess that typified the syndrome. Findings in our patient have buttressed some of their views. Results of tests on the pituitary and its target glands were all normal (Table 1). Although the growth hormone response to insulin-induced hypoglycemia was normal, a 24-hour growth hormone secretory profile and plasma somatomedin C level were not determined. These aspects may still need to be explored in order to characterize the cause of the short stature. Of 54 male patients in the series of Epstein et al,[1] only two were reported as having normal genitalia. All eight patients who underwent testicular biopsy exhibited hyalinzation of the seminiferous tubules with complete absence of spermatogenic activity. Our patient had normal plasma testosterone and prolactin levels with a normal luteinizing hormone and follicle stimulating hormone response to gonadotropin-releasing hormone. Because he was single and was very shy and uncomfortable about discussing sexual matters, semen analysis could not be done.

Epstein et al[1] reported diabetes mellitus in 55 of the 125 cases (44%) they reviewed. The diabetes in Werner's syndrome has been described as mild, ketosis-resistant, and associated with insulin resistance.[4] Recent studies have attempted to delineate the site of receptor abnormality in Werner's syndrome but results have so far been inconclusive.[5] The oral glucose tolerance test and insulin secretory response were normal in our patient (Table 1), but the future development of diabetes cannot be excluded.

Contemporary research on Werner's syndrome has dealt with such aspects as the high frequency of complications following cataract surgery in these patients,[6] the tenfold increase in urinary excretion of hyaluronic acid compared with healthy subjects,[7] and collagen synthesis by cultured fibroblasts from affected patients.[8]

A wide variety of tumors have been reported to occur in patients with Werner's syndrome.[1] Thirteen of the 125 cases (10%) reviewed by these authors had predominantly mesenchymal tumors. Our patient represents the first reported case of a pheochromocytoma due to an abdominal paraganglioneuroma in the context of Werner's syndrome.

Geophagia is the compulsive and intentional consumption of earth. Hawass et al[9] reported three cases, all in females, from Saudi Arabia. Iron deficiency anemia and zinc deficiency, both of which were present in our patient, invariably occur when there is prolonged geophagia.[9-11] This practice probably reflects some element of immaturity or mental subnormality in the patient.

Our case is unique in that it combines three rare clinical problems—Werner's syndrome, an autosomal recessive disorder not previously reported in an Arab, a pheochromocytoma due to an abdominal paraganglioneuroma, and geophagia causing severe iron deficiency anemia.

Acknowledgment

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Letters to the Editor

The *Annals of Saudi Medicine* welcomes letters to the Editor from its readers. They may be on any topic, though the Editor especially encourages discussion of papers published in the *Annals*. Letters should be no more than 100 typewritten lines in length, typed double-spaced, and submitted in triplicate. Letters may include one figure or brief table and up to five references. Submission of a letter constitutes permission for the *Annals* to use it for publication. Letters should not duplicate similar material being submitted or published elsewhere, and the *Annals* reserves the right to edit letters submitted. Letters referring to a recent *Annals* article should be received within 6 weeks of the article's publication.

The Classification of Congenital Factor X Deficiency and Abnormalities

To the Editor: We read with interest the paper on a family with factor X variant by Al-Hilali et al[1] but were surprised that a paper of ours on the same subject was not quoted. Also only one of our papers on factor X defect was quoted, though we have published more than fifty papers on the topic of factor X during the past twenty years. We would like to take this opportunity to propose a suitable classification of factor X defects.[2]

Factor X deficiency was first described in 1956 to 1957.[3-5] Since then, several variants have been described. The factor X Friuli abnormality appears to be the most important and the most extensively studied.[6-9] Recently a peculiar factor X defect with a normal partial thromboplastin time (PTT) was described as occurring on both a sporadic[10,11] and congenital basis.[12] Factor X activity level, in the extrinsic system, was 4.2% in the patient described by Nora et al,[11] 2 to 3% in the patient seen by Bertina et al,[10] and 26 to 34% in the family studied by us.[12] This indicates that the abnormality responsible for the peculiar activation pattern with a defect only in the extrinsic system may present in different forms—severe or moderate. For two of these patients,[10,11] there is no absolute proof of the congenital nature of the defect. Unfortunately, no immunological assay is given for the patient reported by Nora et al,[11] and this further makes a sure classification impossible.[9,13] The patient presented by Bertina et al[10] had an antigen level of 50% of normal. Factor X Padua patients show a level of 100% of normal. The family described by Al-Hilali et al[1] showed a factor X activity of 3% and normal factor X antigen level. However, there is a disturbing feature in the studies presented, namely a concomitant mild reduction in factors II, V, and VII. Apparently factor IX was not tested and no immunological assay of these three factors was available either. These data suggest the existence of a combined defect. Whether this is congenital or due to liver damage, as surmised by the authors, remains to be proved. Because the level of these factors in the family members was not studied, the possibility remains that the defect might be a combined defect (of prothrombin complex factors?). The existence of an abnormal factor X exhibiting peculiar activation patterns must be recognized. The discovery of this peculiar type of factor X deficiency (abnormality limited to the extrinsic system) has considerably complicated the differential diagnosis of factor VII and X deficiencies and abnormalities. In the past an abnormal Russell's viper venom (RVV) clotting time was used to discriminate between factor X and VII deficiency, but we demonstrated this not to be true.[6,7] Factor X Friuli in fact may be normally activated by RVV.[6] A factor X abnormality with prolonged PTT and normal or near normal prothrombin time has also been described.[14,15] In this form the defect seems to lie only or mainly in the intrinsic system. The great heterogeneity of the factor X defect is further emphasized by the recent discovery of an additional congenital factor X variant (factor Padua 2).[16] This variant displays a discrepancy between the levels of factor X obtained by clotting assay and those seen by amidolytic assay. Table 1 summarizes the factor X variants so far described. Other variants may exist, as suggested by the preliminary report of another patient[17] and by other studies.[13] Finally, it is interesting to note that bleeding manifestations varied considerably, namely from severe to none. In general it seems that those patients with defects in all three activating systems showed the most severe bleeding. The extrinsic system appears to be the least important determinant in the bleeding tendency, such that patients with only the defect are asymptomatic.[1,12]

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TABLE 1. *Main features of factor X deficiency and of factor X abnormalities so far described.*

	Factor X assays					
Condition	Tissue thromboplastins (extrinsic)	RVV cephalin (RVV)	Cephalin (intrinsic)	Chromogenic	Immunological assay	Bleeding manifestations
Classic factor X deficiency (Mr. Stuart)[3,4]	Low	Low	Low	Low	Low	Severe
Miss Prower defect[18]	Low	Low	Low	?	Normal	Severe
Factor X Fruili defect (Mrs. Minin)[7,8,19,20]	Low	Normal	Low	Low	Normal	Moderate
Factor X Melbourne[15] (Rome?)[14]	Normal	Normal	Low	?	Normal	Moderate
Factor X Padua[12] (Leiden?, Riyadh?)	Low	Normal	Normal	Low	Normal	None
Factor X Padua$_2$[16]	Low	Low	Low	Lower than clotting assays	Normal	Mild
Factor X red[10]	Low	Low	Low	?	Variably reduced, but higher than clotting counterpart	Variable

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Reply

To the Editor: I was deeply concerned by the letter from Girolami et al regarding our article on factor X+Riyadh. An apology is definitely due to Girolami and his group, as we never came across the article they mentioned. We conducted a thorough computer search, but the article never appeared, nor was it brought to our attention. It was certainly not missed intentionally.

Although the report of our family was published in 1989, we first encountered them in 1981. It subsequently took two years to establish the diagnosis of factor X abnormality, another two years to get the factor X antigen assay, and a further two years before our report was ready to be published.

We did report on this family at the 9th Annual Meeting of the American Society of Hematology in October 1987, though we could not read it at the meeting and the abstract of our report appeared in Supplement 1 of Blood 1987;70:365a.

Again, I apologize for overlooking their publication.

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Guillain-Barre Syndrome and Myocardial Infarction

To the Editor: McDonagh and Dawson[1] reported two cases of Guillain-Barre syndrome that occurred following myocardial infarction. They observed that myocardial infarction as a precipitant of acute polyneuropathy had not been described, but that their cases might represent a chance association. We encountered a similar case of acute polyneuropathy following myocardial infarction.

A 45-year-old Jordanian patient was admitted on 9 December 1986 into the coronary care unit of the Abha General Hospital with severe chest pain that had started 3 hours before admission. He was a known hypertensive, for which he took atenolol. He had smoked about 20 cigarettes per day over the past 25 years.

The electrocardiogram on admission showed acute anteroseptal myocardial infarction with Q waves in leads V_1, V_2, and V_3 and associated ST elevation. Serum creatine kinase values were elevated. His hemoglobin was 171 g/L; hematocrit was 52% (Abha is in a high-altitude region, over 6,500 feet [1950 meters] above sea level). White blood cell count and differential, erythrocyte sedimentation rate, fasting blood sugar, serum creatinine, electrolytes, blood urea, and chest x-ray study were normal.

His clinical course was uneventful and he was discharged home on the ninth hospital day. During his hospitalization he received morphine, diazepam, and propranolol.

Four days after discharge from the hospital, he experienced a tingling sensation in both feet and hands, followed over the next few days by gradual and progressive weakness of the lower limbs. He was re-admitted 18 days after the initial admission.

On admission he complained of paresthesia and weakness of both lower limbs and could not stand or walk without support. Examination confirmed the leg weakness, and no knee or ankle reflexes could be elicited. Plantar reflexes were indifferent, and there were no signs of sphincter, cranial nerve, or upper limb involvement. There were no objective sensory changes. Hemoglobin, white blood cell count, differential, and erythrocyte sedimentation rate were normal. Fasting blood sugar, blood urea, electrolytes, and chest x-ray study were also normal. Lumbar puncture produced colorless fluid under normal pressure; protein was 1.85 g/L and glucose and cell count were normal. Urinalysis was normal. Other causes of the polyradiculopathy such as porphyria, a connective tissue disorder, and vasculitis were excluded.

A diagnosis of Guillain-Barre syndrome was made, and this was confirmed by a neurologist and electromyography. The patient underwent physiotherapy and his condition gradually improved. He was discharged four weeks later and has made a complete recovery.

During the patient's hospitalization we considered the association between the myocardial infarction and the polyneuritis unlikely. However, the similarity between our case and the two reported by McDonagh and Dawson is striking. The interval between the myocardial infarction and the polyneuritis is also similar—between one to three weeks. Precipitating events such as respiratory infections or gastroenteritis are known to precede the polyneuritis by a period of one to three weeks.[2] Because surgical procedures have also been implicated, it may be that any stress, such as myocardial infarction in our case, that lowers the patient's resistance within the vulnerable period could precipitate the disease, the real cause of which remains unknown.

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Non-menstrual Toxic Shock Syndrome

To the Editor: I read with interest the letter by Fahim[1] and would like to describe my own observations in a patient with non-menstrual toxic shock syndrome, with an emphasis on severe hepatic dysfunctions as a complication of the syndrome. My patient made a complete recovery because of early diagnosis and effective treatment.

A 28-year-old Saudi woman presented with abrupt onset of fever, sore throat, vomiting, confusion, generalized erythrodermic blanching rash, and hypotension, two weeks following a full-term vaginal delivery. On the seventh day following admission, her skin rash began to desquamate and she became deeply jaundiced with moderate ascites.

Laboratory investigations showed the following values: hemoglobin, 84 g/L; white cell count, 24.0 × 10^9/L; platelets, 100 × 10^9/L; blood urea, 20.4 mmol/L; creatinine, 210 μmol/L; sodium, 120 mmol/L; calcium, 1.63 mmol/L; and magnesium, 0.5 mmol/L. Liver function tests showed bilirubin, 529 μmol/L; AST 18.1 μkat/L; and ALT, 19.6 μkat, with normal alkaline phosphatase activity. Abdominal ultrasound examination showed a normal gallbladder and biliary tree with moderate ascites. Culture from the vagina showed a concentrated growth of *Staphylococcus aureus*

She was treated with intravenous vancomycin, dopamine, calcium chloride, and fluids (normal saline and crystalloids), and she made a complete recovery. At the time of the patient's discharge, all laboratory values were normal.

This case fulfilled the criteria for toxic shock syndrome. Grossly abnormal liver function values with hyperbilirubinemia, markedly elevated transaminase enzyme activity, and normal alkaline phosphate levels, as seen in my patient, have been reported only for two fatal cases studied by Larkin et al.[2] Physicians should be aware of this complication of hepatic dysfunction in toxic shock syndrome, as early diagnosis, adequate fluid replacement, vasopressor therapy, and appropriate antistaphylococcal antibiotics can prevent fatal outcome.

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Pneumatosis Intestinalis Associated with Gastric Outlet Obstruction and Complicated by Localized Peritoneal Inflammation

To the Editor: We report a case of pneumatosis intestinalis complicated by localized inflammation and associated with gastric outlet obstruction due to peptic ulcer. Although pneumatosis intestinalis can occur in association with a variety of pulmonary and gastrointestinal disorders, an association with gastric outlet obstruction is rare.

A 23-year-old man presented with upper abdominal pain of one year's duration that was associated with occasional vomiting but not hematemesis. On physical examination, his abdomen was noted to be scaphoid with marked tenderness in the right iliac fossa. A roentgenogram of the abdomen, following barium meal, revealed huge dilatation of the stomach with the lower margin reaching down to the pelvis. There was no radiological evidence of bowel perforation. Endoscopic examination revealed that the pylorus was completely obstructed due to ulceration and fibrosis.

Laparotomy confirmed the diagnosis of gastric outlet obstruction due to peptic ulcer and fibrosis. Also, approximately 20 cm of the distal portion of the ileum was found to be covered with multiple, subserosal, gas-filled cysts (Figure 1). Truncal vagotomy, antrectomy, and partial gastrectomy with a Billroth II type of anastomosis were performed, and the diseased segment of the ileum resected using an end-to-end anastomosis.

Microscopic examination of the ileum revealed many subserosal cysts of variable size lined by fibrous tissue, histiocytes, and foreign body giant cells. These cysts were surrounded by considerable inflammatory infiltrate consisting of lymphocytes, plasma cells, eosinophils, and neutrophils. The inflammatory infiltrate was also present on the serosal lining of the bowel. The mucosa, submucosa, and muscularis propria of the bowel showed normal appearance.

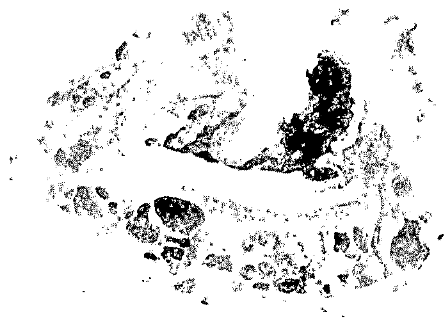

FIGURE 1. Transverse section of the ileum showing pneumatosis intestinalis. Numerous cysts are seen, many of them ruptured on the serosal surface.

The condition in which gross amounts of gas are found within the tissue of the bowel wall has been known variously as pneumatosis cystoides intestinorum, intestinal intramural gas, abdominal gas-filled cysts, and emphysema of the bowel. Because the gas frequently does not remain in the cysts, therefore, the term *pneumatosis intestinalis* is preferred.[1]

Pneumatosis intestinalis was first described by DuVernoy[2] in 1730. It has been found in association with chronic obstructive pulmonary disease, cystic fibrosis, and various types of gastrointestinal disorders such as pyloric stenosis, celiac disease, colitis, and infarction.[3]

Both adults and children are affected by pneumatosis intestinalis, and the course is extremely variable in both, depending on associated conditions. Its etiology is controversial. In the case of peptic ulcer, it is postulated that the gas enters the bowel wall through the mucosal defect and then is distributed by peristalsis. The presence of spaces in the submucosa of the pyloric region adjacent to the ulcer has been documented.[4] In the infantile type of pneumatosis intestinalis the gas is probably produced by bacteria, which later finds its way into the wall of the diseased bowel. The causative theory is different for chronic obstructive pulmonary disease and suggests that air travels along the vascular sheaths in a path of least resistance and ultimately rests on the colonic wall.

Although resection of the bowel in the treatment of pneumatosis intestinalis is controversial when there is no perforation, we resected the involved segment because the patient had tenderness in that region, and the cysts were prominent during operation. These cysts, with inflammatory cells around, were located only on the serosal surface. The muscular layer of the bowel was intact with no evidence of perforation.

Postoperatively, our patient had an uneventful recovery and has done well.

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Laxative-induced Status Epilepticus

To the Editor: We report a case of laxative-induced status epilepticus in a 5-month-old male child. The child was first brought to the emergency room in a drowsy state following administration of 9 drops of Guttalax (a contact laxative preparation) for his constipation given 6 hours before. The prescribed dosage for children between the ages of 2 to 12 years is 2 to 5 drops, diluted in water.

Three hours later, after the child had been admitted to the pediatric ward with a diagnosis of drug overdose, convulsions occurred that were successfully stopped by the administration of valium (2 mg, intravenously) after 2 minutes. The child had no history of convulsions, nor was there any family history of seizures. One hour later, status epilepticus developed that lasted for approximately two hours, and required repeated doses of intravenously administered valium and intramuscularly administered phenobarbital before ceasing.

Following this, the patient's condition improved over 24 hours, and he was discharged home 5 days later with no further episodes of convulsions.

The child was evaluated for possible electrolyte imbalance, metabolic disorders, and infection as the source of the convulsions, but all results of laboratory tests, including repeat biochemical tests and cerebrospinal fluid analysis, were normal. Electroencephalogram and computed tomographic scan of the head were also normal.

Guttalax (picosulfate sodium) is a common contact laxative. Taken by mouth, it stimulates bowel movements, following hydrolysis by colonic bacteria.[1] Cardiac and renal side effects have been reported, but no central nervous system complications have been recorded.

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Book Review

Hodgkin's Disease and Non-Hodgkin's Lymphoma in Adults and Children

LM Fuller, FB Hagemeister, MP Sullivan, WS Velasquez, eds.
New York: Raven Press, 1988
495 pages, $89.00 (US)

This book is based on the collective experience of the University of Texas M.D. Anderson Cancer Center in the U.S.A. in the management of Hodgkin's and non-Hodgkin's lymphoma. This book provides both theoretical and practical information in a format that allows for easy assimilation of the material by medical students and general staff as well as specialized radiation and medical oncologists. There are 22 chapters involving 25 contributors; the editing of this book by a radiation oncologist (Dr. Lillian Fuller), two hematologists (Drs. Fredrick Hagemeister and William Velasquez), and a pediatric oncologist (Dr. Margaret Sullivan) has ensured a balanced opinion throughout the book.

The book is composed of sections on Hodgkin's disease and non-Hodgkin's lymphoma, which are preceded by a comprehensive section giving the essential background information on these diseases. This section includes important chapters on histopathological classifications, immunological considerations, and characterizations of lymphoma in relation to the basic evaluation of the disease process and its extent as determined by diagnostic radiological measures as well as laparotomy staging. The chapter on the effects on gonadal function of chemotherapy and radiotherapy is an asset to this book. Some challenging problems are discussed in the last chapter, including management of the patient with relapsing and refractory disease and the use of bone marrow transplant as a salvage therapy. The chapter on immunodeficiency in relation to lymphomatous disease gives a very up-to-date perspective and is extremely informative.

The book in general is a comprehensive reference on both Hodgkin's and non-Hodgkin's lymphoma in adults and children, therefore bridging a gap often not covered. It should prove a good reference for general clinicians as well as specialized oncologists.

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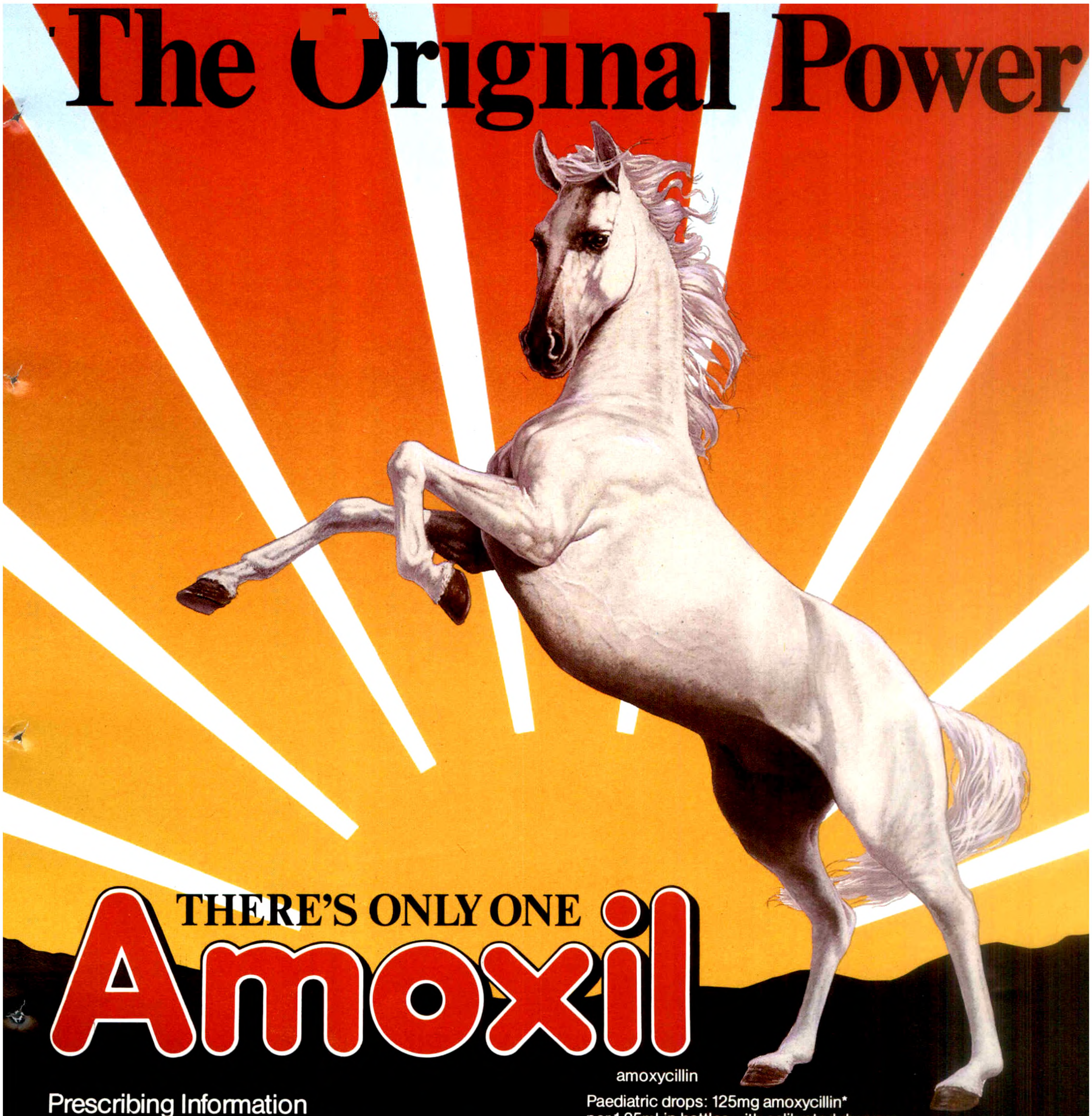

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*as the trihydrate.

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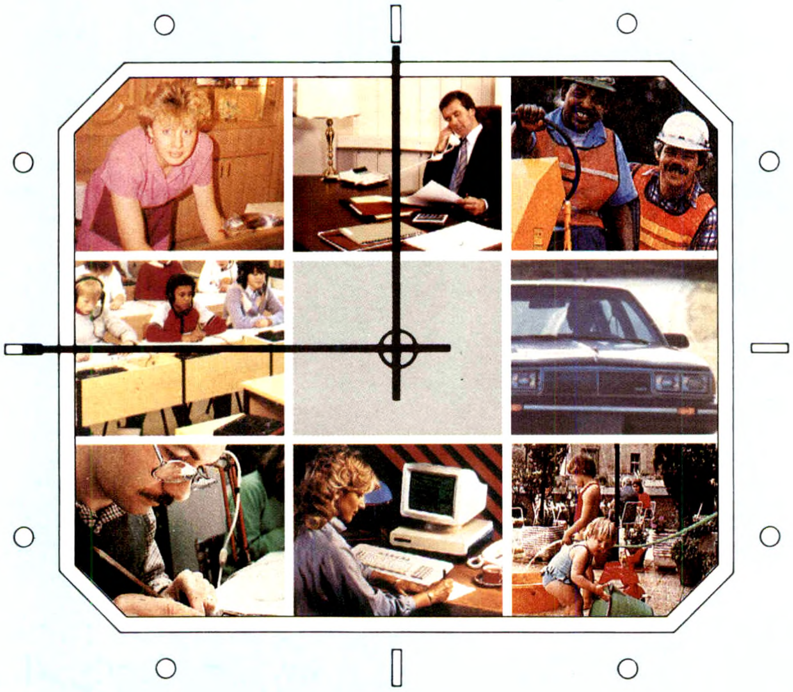

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Symposium Abstracts

FOURTH ANNUAL PEDIATRIC SYMPOSIUM

Sponsored by the Joint Board for Postgraduate Medical Education
King Fahad National Guard Hospital
19-20 Shaban 1409 (26-27 March 1989)

PATHOGENESIS AND MANAGEMENT OF CHRONIC DIARRHEA IN INFANTS AND CHILDREN, F Ghishan, Department of Pediatric Gastroenterology, Vanderbilt University, Nashville, Tennessee, U.S.A.

Chronic diarrhea, accompanied by malabsorption and malnutrition, is a major health problem throughout the world. Most episodes of diarrhea during infancy and childhood are acute and self limited. However, prolonged diarrhea with malabsorption is one of the major causes of childhood malnutrition and can be associated with secondary growth failure and developmental delay. Prolonged diarrhea in early infancy has been defined as an illness with excessive stool water lasting at least two weeks. In older infants and children, four weeks of diarrhea constitute an acceptable definition. Chronic nonspecific diarrhea (Toddler's diarrhea), although the most common cause of persistent loose stools in infants, is not associated with malabsorption and is benign. The pathogenesis of chronic diarrhea is related to alteration in the intestinal function and nutritional status of the patient. The pathophysiological mechanisms causing diarrhea are: genetic factors resulting in loss of a carrier or enzyme; secretory diarrhea resulting from increased production of enterotoxin, hormone, and deconjugation of bile salts; decreased surface area resulting from short bowel and celiac disease; and delayed intestinal motility such as pseudo-obstruction syndromes. These abnormalities result in diarrhea leading to varied degrees of malnutrition. Malnutrition delays the repair and adaptation of the intestinal epithelium, resulting in a vicious circle of chronic diarrhea—malabsorption—malnutrition—chronic diarrhea. Evaluation of patients should be directed at adequate nutritional assessment coupled with identification of the pathogenic factors. Stool examination for the presence of white and red blood cells, reducing substances, fat, ova and parasite, stool osmolality, and electrolytes should form the foundation upon which other tests are performed. Understanding of the alteration in the digestive and absorptive function of the intestinal epithelia in patients with chronic diarrhea emphasized the role of enteral nutrition utilizing casein hydrolysate, medium-chain triglycerides, and polycose as sources for protein, fat, and carbohydrates, respectively. Enteral rather than parenteral feeding results in stimulation of various trophic factors which are essential for the repair mechanism of the intestinal tract. Patients who fail to respond to enteral feeding are managed by total parenteral nutrition for a period of three to four weeks, with gradual introduction of enteral feedings. Pharmacological therapy should be restricted to specific disease entities.

MEASLES IN RIYADH CITY: MEASLES VACCINE FAILURE, A Abanamy, H Salman, M Khalil, M Abdulazim, Suleimania Children's Hospital, Riyadh

During the last few years, many cases of measles in previously vaccinated children have been reported. In order to study measles vaccine failure, 336 measles cases were included in a descriptive study conducted in Suleimania Children's Hospital. Measles was diagnosed clinically and serologically using measles fluorescent IgM. The analysis and interpretation of data were discussed. Of the patients with measles, 29.4% had been vaccinated. This percentage, although outwardly high, seems to be within normal, considering the seroconversion following the vaccination at the age of nine months and the coverage rate of the measles vaccination. The seroconversion rate was about 85% at the age of nine months. No significant difference between the levels of maternal antibodies was found at the age of six and nine months. The main cause of the failure of the measles vaccine was a primary type of vaccine failure due to the persistence of maternal antibodies. The failure of measles vaccination due to a possible defect of the cold chain was almost excluded by testing samples of vaccine collected from various health centers in Riyadh. The need for adjusting the measles vaccination schedule is suggested by the results of this study.

CONGENITAL HEPATIC FIBROSIS, AMA Abdullah, S Nazer, M Attiyah, MA Ali, Departments of Pediatrics, Medicine, and Pathology, King Faisal Specialist Hospital and Research Centre, Riyadh

Congenital hepatic fibrosis (CHF) is a recognized cause of portal hypertension with esophageal varices in children. We studied the varied clinical presentation of CHF as seen at KFSH&RC in order to provide referring pediatricians with essential criteria for the diagnosis of CHF. Fourteen children with CHF were diagnosed during 1981 to 1988. Their ages at presentation ranged from 21 months to 14 years (mean; 7.5 years). Clinical manifestations at diagnosis were (number of children), splenomegaly (12), hepatomegaly (11), growth failure (10), marked abdominal distention (4), and fever (4). Liver function tests were essentially normal except for high alkaline phosphatase activity. Eight patients had polycystic kidney disease confirmed by ultrasound. Upper gastrointestinal endoscopy showed esophageal varices in all seven patients examined. Splenoportography demonstrated splenic vein occlusion in one patient. CT scan of the brain confirmed an arteriovenous malformation in a patient who presented with an encephalitis-like picture. This patient subsequently died of aspiration pneumonia. One patient was lost to follow-up. The remaining 12 patients are alive and are on regular follow-up. One patient has required splenorenal shunt. In view of the relatively common finding of hepatomegaly and normal liver function tests among Saudi children, it is essential that CHF be considered in the diagnosis of such children, especially in the presence of renal anomalies and/or evidence of portal hypertension. Diagnosis of CHF was confirmed histologically in all 14 patients.

OUTPATIENT MANAGEMENT OF CHILDHOOD DIABETES: EXPERIENCE OF A PEDIATRIC DIABETIC CLINIC AT KKUH, MA Abdullah, King Khalid University Hospital, Riyadh

This paper presents the first four years' experience of a pediatric diabetic clinic which was established in 1983 and operated by a team. Sixty children below 12 years of age were registered during this period, 34 (56.7%) males and 26 (43.3%) females; 41 (68.3%) were Saudis and 19 (31.7%) were non-Saudis. Fifteen (25%) were from upper, 32 (53.3%) from middle, and 13 (21.7%) from lower social classes. Fourty-six percent of the mothers were illiterate. All patients and their parents were given an educational program at first contact and thereafter. Even illiterate parents could be trained easily. Variations in the availability of insulin and/or insulin syringes created confusion among parents. Dietary misconceptions were common, and dietary instructions were more difficult to impose than found in other studies, as a result of which almost 31.1% of children were on free diet. Almost 94% of patients were trained on home blood glucose monitoring. Of 45 patients analyzed, 26 (61.9%) were doing it regularly, 12 (28.6%) were irregular, and four (9.5%) stopped completely. Urine testing was done somewhat regularly by all patients. The mean HbA_1 in the patients was 11.5%. Parent training and a phone-in system reduced hospital admissions of patients with hypoglycemia and ketoacidosis. Chronic complications were not encountered among the study group. Diabetic children should be looked after by trained pediatricians. Adolescents should be seen in combined clinics by adult physicians. Establishment of regional referral pediatric diabetic clinics is recommended. More emphasis should be put on parent education in addition to training of general practitioners. Local Arabic-speaking diabetic nurse educators should be trained. All monitoring and treatment tools should have instructions written in Arabic. Insulins and insulin syringes should be standardized throughout Saudi Arabia. Dietary instructions should be realistic. Multitest urine testing strips should be avoided. Blood sugar testing meters with no local agents or maintenance facilities should be discouraged. Facilities to measure HbA_1 should be made available at regional levels. Further nationwide studies to assess the magnitude of the problem and the local management problems are recommended.

CHRONIC LIVER DISEASES IN CHILDREN, F Ghishan, Department of Pediatric Gastroenterology, Vanderbilt University, Nashville, Tennessee, U.S.A.

Liver disease in children is generally secondary to infectious, metabolic, toxic, or autoimmune factors. Clinically, the presenting symptoms are unique to each age group. The neonate has a tendency to develop cholestatic jaundice secondary to immaturity of the bile acid transporting mechanisms across the plasma membranes of the enterocytes and hepatocytes. Thus, metabolic or infectious causes can result in a similar cholestatic pattern. Older children with liver disease may have a nonspecific presentation. Of the infectious agents, hepatitis B virus (HBV) remains one of the major causes of morbidity and mortality worldwide. Transmission of hepatitis B during the perinatal period results in the most serious consequences of HBV infection, and 90% of infected infants become chronic carriers. These HBV carrier children have a 25% lifetime risk of dying from primary hepatocellular carcinoma or cirrhosis during adulthood. Treatment of newborns at risk with a combination of hepatitis B immunoglobulin and hepatitis B vaccine is 85 to 95% effective in preventing development of the HBV chronic carrier state. Non-A, non-B hepatitis similarly can lead to a chronic carrier state and is transmitted vertically to newborns. Unfortunately, this transmission cannot be prevented. In older children, chronic hepatitis of the autoimmune type is seen more frequently than hepatitis. This disease is classically responsive to immunosuppressive therapy. Metabolic disorders resulting in chronic liver injury include inborn errors of carbohydrate metabolism (glycogen storage disease, galactosemia, and fructose intolerance), inborn errors of protein metabolism (tyrosinemia), inborn error of fat metabolism (acid cholesterol ester hydrolase deficiency), inborn errors of porphyrin metabolism (protoporphyria), inborn errors of bile acid metabolism, inborn errors of copper metabolism (Wilson's disease), and unclassified inborn errors such as alpha-1-antitrypsin deficiency and cystic fibrosis. The use of the Menghini needle biopsy for histological and biochemical evaluation of liver tissue has allowed accurate diagnosis in many of these disorders. Management of these inborn errors depends on nutritional therapy (i.e., carbohydrate and protein metabolism) or drugs (Wilson's disease). Liver transplantation is no longer an experimental approach for the treatment of life-threatening end-stage liver disease in infants and children with untreatable metabolic disorders.

BRONCHIOLITIS DURING THE WINTER MONTHS OF 1987-1988 AT KING FAHAD NATIONAL GUARD HOSPITAL, RIYADH, AA Adeyokunnu, S Al-Seayed, Department of Pediatrics, King Fahad National Gaurd Hospital, Riyadh

Following the clinical impression of an outbreak of bronchiolitis during the winter months October 1987 through February 1988 at our hospital, a retrospective analysis of cases was carried out to determine its extent in relation to other acute respiratory problems (ARP), attendant morbidity and mortality, and challenges ahead. Of the 932 children admitted during the study period, 235 (25%) had ARP and 32 (14%) of these were cases of bronchiolitis. In the preceding winter months (1986/1987), the total admissions were 750, 117 (21%) for ARP, 5 (4%) of which were for bronchiolitis. The 32 patients with bronchiolitis (19 M, 13 F), aged two to 44 weeks (mean, 11 weeks), had a mean hospital stay of nine days (range, three to 32 days). There were no deaths but morbidity based on complications, length of hospitalization, need for invasive procedures, and intensive care management was 15% (5/32), a rather high figure compared with other published figures. The data collated confirmed the clinical impression. Use of tests specific to respiratory syncytial virus, a main pathogen of bronchiolitis, poses a diagnostic challenge requiring a concerted approach for a solution: ribavirin was not used in any of our patients. We are aware of its qualified role in the effective management of bronchiolitis. Its future use constitutes our therapeutic dilemma.

AGE AT MENARCHE OF SCHOOLGIRLS IN SAUDI ARABIA, ASIR REGION, WITH A NOTE OF THEIR HEIGHTS AND WEIGHTS, NL Attalah, King Faisal Military Hospital, Khamis Mushayt

Data on age at menarche have been collected from 1011 Saudi girls attending four different schools within King Faisal Military Cantonment, Khamis Mushayt, Asir Region. The girls represented two different groups classified arbitrarily according to family size. The mean ages, estimated by probit analysis, were 13.07 ± 0.16 years for small family size and 13.81 ± 0.15 years for the large families. The results were compared with data reported from other Arabic countries and with that from other populations. Girls from small families representing the upper middle class of the community, have one of the earliest recorded means of all African and Asian populations studied. Compared to Europeans, adult Saudi girls, with a mean height of 153.7 cm and mean weight of 53.0 kg, were found to be significantly shorter and lighter by an average of 8.8 cm and 4.5 kg, respectively. It seems likely that Saudi girls, if brought up under good environmental conditions and family planning, may be as early in their maturation as girls in Central and Southern Europe. The menarchal age in girls from different regions of the Kingdom of Saudi Arabia, urban, rural, and at sea level, remains to be determined, as well as the effect of the environment and altitude on maturation. It is also very important to investigate age at menarche from generation to generation at appropriate intervals for the evaluation and monitoring of any national health program. By improving the socioeconomic status and health care in the community, children grow bigger, have a faster tempo of growth, and enter puberty earlier to attain their genetic potentials for growth.

COMBINATION CHEMOTHERAPY FOR CHILDREN WITH NEWLY DIAGNOSED ACUTE LYMPHOCYTIC LEUKEMIA: ALL-KFSH-87 PROTOCOL, RJ Aur, M Hanna, K Sackey, R Sabbah, H Tufenkeji, G Roberts, K Sheth, S Willoughby, J Atwood, King Faisal Specialist Hospital and Research Centre, Riyadh

This study was designed to test combination cheeuherapy (ChemoRx) to attain cure. It was derived from ALL-KFSH-84 Protocol *(Ann Saudi Med* 1987;7:13-22 with pulses of VM-26/Ara-C, asparaginase/Ara-C, and prednisone (Pred)/vincristine (VCR)/daunomycin (Dauno) given, respectively, at 4, 8, and 12 months. Induction consisted of Pred, VCR, Dauno, VP-16, and IT methotrexate (MTX) for 6 weeks, followed by 2-year maintenance with PO mercaptopurine and PO and IT MTX/IT MTX + Ara-C + hydrocortisone. From 1 January 1987 to 15 November 1988, 57 children four months to 14 years; 36 boys, 21 girls were entered into the study. Initial WBC count was 1300 to 340,000 mm^3 (median, 9,600); two patients had mediastinal mass (one also had CNS leukemia) and three had testicular leukemia (two bilateral). Current outcome of the 57 patients is: four in induction Rx phase, three died of infections during induction phase, and 50 attained complete remission (one with backup Rx). Of these, one died during maintenance (5 months), one abandoned Rx in complete remission, seven developed hematologic relapse (4 months (5), 7 and 19 months), and 41/50 (82%) are in continuous complete remission for 1 to 22 months. Initial features of the seven relapsed patients were provided. These 23-month results indicate that this combination ChemoRx is effective in inducing complete remission and in maintaining continuous complete remission in children with acute lymphocytic leukemia.

TREATMENT OF TYPHOID FEVER WITH A THIRD-GENERATION CEPHALOSPORIN CEFTRIAXONE, A Abanamy, H Salman, M Shuja, M Cheriyan, Suleimania Children's Hospital, Riyadh

Ceftriaxone, a broad-spectrum third-generation cephalosporin with markedly long half-life, has been used recently in *Salmonella* infections, especially in typhoid fever resistant to usual antibiotics (ampicillin, chloramphenicol, cotrimoxazole). Ten children who were moderately to severely ill with typhoid fever (proved bacteriologically and seriologically) were treated in Suleimania Children's Hospital, Riyadh, with a single daily intravenous injection of ceftriaxone. All children improved clinically after 48 hours. All became afebrile within three to five days. There was no failure; one patient treated for five days suffered relapse (positive blood culture and sensitivity) one week after stopping therapy but was cured with a second course of ceftriaxone. We conclude that ceftriaxone is a good alternative antibiotic for the treatment of *Salmonella* infections because of its activity, simplicity of administration (one or two injections per day), and reduction of hospitalization and cost.

CONGENITAL DISLOCATION OF THE HIP: THE SAUDI ARABIAN EXPERIENCE, MR Beg, King Fahad National Guard Hospital, Riyadh

The terminology concerning congenital dislocation of the hip should now be changed to congenital dysplastic hip (CDH) because it is dysplasia that leads to dislocation. CDH in Saudi Arabia is common. My experience with this disorder at King Fahad Hospital is described, along with our methods of screening and treatment, with particular reference to the type of populations and problems we face. One hundred seventy-five cases were seen in the last five years. From a treatment point of view dislocatable hips were treated along the same lines as dislocated ones. Of a total of 13,398 live births, 110 cases were diagnosed and treated. The incidence comes to 8:1000. This series of 175 cases also includes 65 neglected cases referred from elsewhere. The practice of swaddling the baby and marriage between first cousins is common in our population. Both factors contribute to the high incidence in this series. Marriage counseling and educational campaigns against swaddling can reduce the incidence of CDH in Saudi Arabia.

ACUTE SEPTIC ARTHRITIS OF THE HIP IN INFANCY AND CHILDHOOD, O Bennett, Dammam Central Hospital

Twenty-seven children with septic arthritis of the hip treated at Dammam Central Hospital between 1983 and 1987 are analyzed: 20 (74%) were five years or younger. *Staphylococcus aureus* was the most common pathogen isolated and over 55% of the strains were penicillin resistant. Children who received treatment within six days of the onset of the symptoms had a satisfactory prognosis compared with the remaining children. The key to a successful outcome is early diagnosis, immediate surgical decompression and debridement of the hip, immobilization of the hip, and antibiotic therapy. The diagnosis may be difficult to establish, especially in neonates and infants who do not exhibit the classic physical signs and symptoms.

HYPOXIA IN CHRONIC LIVER DISEASE, S Al-Dusari, BG Loftus, JF Price, AP Mowat, Department of Child Health, King's College Hospital, London, England

Hypoxia, probably due to pulmonary arteriovenous shunt formation, is a recognized complication of liver cirrhosis in adults. Liver transplantation is contraindicated in the presence of hypoxia. No estimates of the frequency of this complication in childhood are available. We have studied 36 children with chronic liver disease. Clinical and biochemical data were recorded, and oxygen saturation was measured using a Biox 3700 oximeter. Arterial blood gases were measured if saturation was less than 95%. There were 12 boys and 24 girls, aged 0.2 to 15 years (mean, 6 years). Seventeen had biliary atresia; six, alpha-1-antitrypsin deficiency; 6, hepatic fibrosis; 2, chronic active hepatitis, and five, other diseases. Prothrombin time was prolonged in 29, albumin was low in seven, and 12 had proven varices. Five children were hypoxic. Clubbing and cutaneous shunts were more prevalent in hypoxic children. Hypoxia is relatively common in chronic in liver disease.

CHILDHOOD BRUCELLOSIS IN RIYADH, YA Al-Eissa, AM Kambal, FA Al-Zamil, NM Al-Jishi, King Khalid University Hospital, Riyadh

Brucellosis is a major public health problem in Saudi Arabia. The scarcity of childhood brucellosis reports served as the impetus for this retrospective study. The case records of 102 consecutive cases, with a proven diagnosis of brucellosis seen between January 1984 and December 1987 were reviewed. There were 52 boys (51%) and 50 girls (49%). Ages ranged from 1½ months to 14 years (mean, 7.1 years). Ninety-eight percent of the patients were Saudis and 70% were from Riyadh city. Raw milk ingestion was noted in 70.6% and a family history of brucellosis was positive in 62.7% of the patients. Fever, arthralgia, malaise, and weight loss were the common presenting complaints, occurring in 91%, 72.5%, 60%, and 48%, respectively. Arthritis, splenomegaly, hepatomegaly, and lymphadenopathy were found in 37%, 35%, 28%, and 15.7%, respectively. Osteomyelitis was noted in two cases. Positive blood cultures for *Brucella* were detected in 63 (72%) of 87 tested patients. Various combinations of antibiotics, including co-trimoxazole, tetracycline, rifampin, and streptomycin, were used. Eighty-five patients had regular follow-up and 17 (20%) of these relapsed. The incidence of brucellosis in children appears higher than is generally realized. Appropriate antibiotic regimens with adequate dosage and duration and regular follow-up will significantly reduce morbidity and complications. Public health education concerning the hazard of raw milk ingestion cannot be overemphasized.

ALLERGENS IN SAUDI HOMES IN RIYADH, AR Al-Frayh, King Saud University, SM Hasnain, King Faisal Specialist Hospital and Research Centre, Riyadh

In order to identify an evaluate the indoor allergens in Saudi homes possibly responsible for perennial asthma and rhinitis, a study was conducted in Riyadh involving biochemical analysis of dust and exposure of Czapek's Dox Agar plate in the indoor environment of 180 asthma and rhinitis patients and 27 control subjects. The study revealed that 95% of the homes were positive for allergenic fungi, 70% for cockroach protein, and 14% for rodent urine. These were present in house dust. Dust mites appeared to be nonexistent. While there were no specific correlations, the general pattern indicated higher allergenic components in asthmatic homes than in control homes. In fungal culture, *Aspergillus* and *Alternaria*, two highly allergenic species, constituted 35.8% and 29.7% in asthmatics' environment, respectively, compared to 22.2% and 18.5% in control homes. *Penicillum* was the most common. Diagnostic skin testing conducted on a heterogeneous group of patients with both seasonal and perennial manifestation of symptoms indicates strong or moderate positive reactivity with commercially prepared antigen from cockroach and fungi along with pollen and outdoor allergens. Antigen preparations using local varieties and species are under way for more specific diagnosis of asthmatic patients.

PATTERN OF VIRUS ISOLATE IN CHILDREN WITH ACUTE RESPIRATORY TRACT INFECTION IN KHARTOUM (SUDAN), MS Hashim, AE El-Haq, Department of Paediatrics, Faculty of Medicine, University of Khartoum, Khartoum, Sudan

The chief causes of morbidity and mortality among children are diseases of the respiratory system, malnutrition, and diarrheal diseases followed by measles, malaria, bilharzia, and tuberculosis. Sudanese children are particularly susceptible to pneumonia and other widespread infectious diseases. The magnitude of the problem of acute respiratory tract infections is illustrated by the fact that respiratory diseases are the chief cause of mortality and morbidity in children, and that those under five years of age are most vulnerable. The information on morbidity and mortality has been obtained mainly through analysis of hospital statistics and other official reports. The present study includes a few hundred children with respiratory tract infection admitted to the Children's Hospital of Khartoum. Forty-four patients were positive for specific viruses, out of 816 children admitted. Thus, the positive isolates represented only 5%. Adenovirus was isolated in 36%, polio, 21%; HSV, 14%; COXB, 11%; RSV, 8%; ECHO, 8%; parainfluenza, 1%; and mumps, 1%. More cases were seen in winter: January, 46%; February, 34%; March, 14%; 32% occurred in infants, 34% in age group 1 to 4 years and only 22% in age group 5 to 9 years. The mean age of these groups was 5.4 months, 2 years, and 6.3 years, respectively. No bacteriological studies were done and all patients received parenteral antibiotics. The patients were not followed long enough and no serological tests were done; no deaths or later complications were recorded. There is a need for community-based studies and longer follow-up. Sensible administration of antibiotics should be observed.

PRESENTATION OF SEVERE "CHLOROQUINE RESISTANT" FALCIPARUM MALARIA IN SUDANESE CHILDREN, MS Hashim, Department of Paediatrics, Faculty of Medicine, University of Khartoum, Khartoum, Sudan

Malaria in Sudan is still a leading cause of mortality and morbidity in children. It is the primary reason for outpatient attendance and hospital admission. However, during the last two years, a particularly severe pattern of presentation has been observed. All cases occurred in children under five years of age. The illness was usually of a few weeks' duration, but patients had a past history of definite or clinical malaria for which chloroquine, in standard doses was prescribed. All patients presented with fever, moderate or marked anemia, grossly enlarged spleen (at or below the umbilicus), and hepatomegaly. Three of the 15 children had generalized lymphadenopathy, with significant enlargement, particularly the cervical groups. Peripheral blood showed leukoerythroblastosis. The children were not jaundiced and urine contained no urobilinogen. Most had received parenteral chloroquine before hospital admission. In nine cases, acute leukemia was suspected. Infectious mononucleosis and lymphoma were considered in the other six cases. However, the Paul-Bunnell test was negative. Bone marrow aspirate was examined in five cases; the marrow was active and cellular. Lymph node biopsy was examined in two patients; the histopathology showed nonspecific hyperplasia. However, all investigations confirmed that malaria was the cause of this pattern of clinical presentation. All patients responded well to Fansidar (sulfadoxine plus pyrimethamine).

CLINICAL MANIFESTATION AND MOLECULAR PATHOLOGY OF SICKLE CELL DISEASE, MAF El-Hazmi, College of Medicine, King Saud University, Riyadh

Sickle cell disease (SCD), a genetic abnormality, is clinically recognized as a multisystem disorder Pauling et al in 1949 characterized the disease as a molecular disorder resulting from a change in the normal sequence of amino acids (i.e., replacement of glutamic acid by valine in the beta chain of HbA). Following the introduction of recombinant DNA technology, molecular biology studies at the gene level led to the precise definition of the molecular pathology of the disease (i.e., CTC is converted to CAC). More recently, the Southern blotting technique has been applied extensively for the study of biochemical genetics and for investigation of genetic polymorphisms, which showed wide variations of the polymorphic pattern among different populations. In Arabia, SCD has a high prevalence in some regions of Saudi Arabia and presents with a variable degree of severity, ranging from mild to one that is as severe as that reported in the majority of other populations. In an effort to better understand the molecular pathology of the two forms of the SCD, we investigated the beta-globin gene region using Southern blotting with different restriction endonucleases in patients presenting with mild and severe SCD. Xmn I polymorphic site and beta-globin gene haplotypes were found to be significantly different in patients from different regions of Saudi Arabia. The clinical, hematological, and molecular patterns obtained in the SCD patients with different forms of the disease was presented and correlated with the beta-globin gene haplotypes encountered in different regions of Saudi Arabia.

NATURAL HISTORY OF SICKLE CELL DISEASE IN SOUTHWESTERN SAUDI ARABIA, MAF El-Hazmi, MA Babiker, H Bahakim, AM Al-Sowailem, AS Warsy, King Saud University and Central Children's Hospital, Riyadh

Using a prospective and retrospective approach, the natural history of sickle cell disease (SCD) was investigated in 50 children from the southwestern province of Saudi Arabia. Height, weight, and head circumference were measured and physical examination was carried out to assess involvement of the cardiovascular, respiratory, skeletal, genitourinary, and central nervous systems. Relevant hematological and biochemical analytes were determined. The patients were followed for two to five years and the information obtained was recorded on special forms. The severity of the disease was assessed and severity index was calculated for individual patients. Results showed two major forms of SCD. Some patients exhibited a mild form while others were severely affected, showing signs of hand and foot syndrome, repeated crises, and the need for frequent blood transfusions. The results obtained in the two groups were presented and the natural history of sickle cell disease in the southwestern province discussed. Though the benign form generally does not require emergency treatment, the severe form is frequently encountered in the accident and emergency department. Recent trends in the management of SCD crisis was outlined and adoption of general guidelines advocated.

SPONTANEOUS ESOPHAGEAL PERFORATION IN A NEWBORN, AJ Jawad, AM Al-Muzrachi, AI Al-Samarrai, Division of Paeditric Surgery, Department of Surgery, King Khalid University Hospital, Riyadh

Due to aggressive resuscitation and supportive measures in neonatal intensive care units, especially for preterm neonates, a new complication, esophageal perforation, has emerged. Despite the large number of neonatal resuscitations, iatrogenic esophageal perforation is still uncommon. Generally the condition goes unrecognized until the signs of respiratory distress or upper esophageal obstruction appear, mimicking esophageal atresia. Esophageal perforation in the adult is a serious problem requiring urgent surgical intervention, while in the neonate a nonoperative approach has been adopted by many authors with good results. A case of spontaneous cervical esophageal perforation forming a pseudodiverticulum in a 3.6 kg neonate who presented with poor sucking and fever is reported. The diagnosis was confirmed by chest x-ray study. Eighty-three reported cases of transesophageal perforation were reviewed; pseudodiverticulum of the esophagus was documented in only 9 of the 83 reported cases. Fourteen had spontaneous esophageal perforation.

CHILDHOOD SHIGELLOSIS: 4-YEAR EXPERIENCE AT KING FAHAD NATIONAL GUARD HOSPITAL, RIYADH, AF Kagalwalla, S Al-Alola, S Khan, H Yaish, King Fahad National Guard Hospital, Riyadh

A total of 114 consecutive isolates of *Shigella* were cultured from the feces of 114 children seen at the King Fahad National Guard Hospital between January 1985 and December 1988. There were 65 boys and 49 girls, with age ranging from 2 days to 13 years (mean age, 3.5 years). Sixty-six patients were hospitalized while the remaining 48 were treated as outpatients. Diarrhea was present in 103 of 114 (91%) patients. Vomiting and fever were each seen in 79 (70%) of patients. Forty-one percent (36%) of the cases had bloody diarrhea; convulsions were recorded in 13 (12%) of the patients. *Shigella flexneri* was isolated in 54 of 114 (47%) of the *Shigella* isolates, *Shigella sonnei* in 40 (35%), *Shigella boydii* in 18 (16%), and *Shigella* dysenteriae in 1 (0.9%). All isolates were sensitive to nalidixic acid, but 47 (42%) were sensitive to ampicillin and 43 (38%) to trimethoprim-sulfamethoxazole. *Shigella* gastroenteritis is usually a self-limiting illness. Antimicrobial agents shorten the duration of illness in moderate to severe cases. Ampicillin or trimethoprim-sulfamethoxazole are the recommended antimicrobials, but with increasing resistance to both these drugs, alternate agents to the suggested regimen are recommended.

CHILDHOOD BRUCELLOSIS IN SAUDI ARABIA,

AF Kagalwalla, S Khan, S Al-Alola, MY Khan, HM Yaish, King Fahad National Guard Hospital, Riyadh

A retrospective analysis of 84 consecutive patients treated for brucellosis at the King Fahad National Guard Hospital from January 1984 to December 1988 was done. Diagnosis was based on a *Brucella* agglutination titer of 1:160 or more and/or a positive *Brucella* culture. The mean age of the patients was 7 years and there were 49 males and 35 females. Fifty-eight patients were hospitalized and the remaining 26 were managed as outpatients. A history of raw milk ingestion was obtained in 64% and there was a positive family history for brucellosis in 39%. The predominant presenting complaints were joint pains in 62% and fever in 90%. Splenomegaly was present in 25% and hepatomegaly in 21%. The sedimentation rate was increased in 83% and bacteremia was documented in 47.7% of the children who had a blood culture done. A triple-drug regimen was used in 43% of the patients, two-drug therapy in 49%, and a single drug was employed in 3% of the patients. Treatment consisting of co-trimethoxazole and rifampin was the most common. Triple-drug therapy that included streptomycin was administered in a significant number of patients. An overall relapse rate of 14% was noted for the entire study group. We conclude that the incidence of brucellosis is increasing in children and that the disease is more common than previous studies have shown. A high index of suspicion is needed for its early recognition and treatment. Streptomycin and tetracycline have been found to be highly efficacious in adults; however, dental toxicity limits the use of tetracycline in children to those over 7 years of age, and streptomycin can only be given parenterally. Prospective studies in children are warranted to test the efficacy of other antimicrobial combinations.

PULMONARY MECHANICS OF INFANTS WITH TRANSIENT TACHYPNEA OF NEWBORN COMPARED WITH HEALTHY TERM INFANTS,

S Khan, GS Ahmed, A Abu-Taleb, King Fahad National Guard Hospital, Riyadh

Currently there is limited data on the pulmonary function of newborns, particularly those with respiratory disorders. A prospective study was performed to assess pulmonary function of healthy full-term infants (HF; N = 17) and infants with transient tachypnea of newborn (TTNB; N = 23). The pulmonary function tests (PFTs) were performed without sedation on infants breathing spontaneously. A facemask attached to a Fleisch pneumotachometer (00) was used to measure flow rates. Transpulmonary pressures were determined by comparing esophageal pressure (equivalent to pleural pressure) to airway pressure. The flow and pressure signals were digitized, stored, and analyzed on an IBM compatible computer. The mean PFT values for each group were reported. The results of the HF group are similar to published values for other populations. There were no significant differences in lung compliance or airway resistance between the two groups. As expected, the TTNB group had significantly shorter IT, ET, Ti/T, and higher peak expiratory flow. We conclude that (1) healthy Saudi newborn infants have similar pulmonary function values as reported in the literature; (2) the TTNB group has higher frequencies leading to shorter IT, ET, Ti/T, and higher peak expiratory flow; and (3) by the mean age of 28 hours, when the TTNB group was tested, there was no significant difference in the breathing between the groups, suggesting that the TTNB group should have a good respiratory prognosis.

IS ROUTINE NEONATAL SCREENING FOR GLUCOSE, CALCIUM AND MAGNESIUM WARRANTED IN LARGE-FOR-GESTATION TERM INFANTS?,

J Ellis, S Khan, GS Ahmed, H Yaish, Department of Pediatrics, King Fahad National Guard Hospital, Riyadh

In Western countries, large-for-gestation (LGA) infants are known to be at increased risk for hypoglycemia and hypocalcemia which often require treatment and may occasionally be life-threatening. It has been recommended that LGA infants have routine screening of glucose, calcium (Ca), and magnesium (Mg). A prospective study was carried out to determine the incidence of hypoglycemia, hypocalcemia, and hypomagnesemia in Saudi newborns delivered at King Fahad Hospital in Riyadh. During a one-year period from 1 April 1987 to 31 March 1988, all LGA infants (N = 180; birth weight, > 4 kg) were screened for glucose, Ca, Mg, and hematocrit. The results were compared with normal values derived from a concurrent study of glucose, Ca, and Mg values determined in a group of full-term Saudi, appropriate-for-gestational age (AGA) newborns (N = 82). Student's t test was used to compare the means and chi-square analysis for discrete variables. The LGA group had an 11.1% incidence of hypoglycemia (dextrostix, < 45 mg/dl) versus 2.4% in the control AGA group. There were no cases of hypocalcemia (Ca, < 7 mg %) in either group. The mean Ca and Mg levels were significantly lower in the LGA group, though within the range of normal. The LGA group had significantly higher birth weight, length, ponderal index, male sex, maternal age, cesarean section rate, and infants with diabetic mothers (IDMs). No significant differences were found in the incidence of fetal distress or meconium staining. At 24 hours of age, the subset of LGA/IDM infants was found to have Ca levels that were near the lower limits of normal and mean Mg level was subnormal (1.48 mg/dl). We conclude that LGA Saudi infants are at increased risk for hypoglycemia compared with AGA infants and should have routine glucose screening. However, screening for hypocalcemia and hypomagnesemia is probably not warranted except in infants born to diabetic mothers.

EFFECTS OF MALIGNANCY ON PREGNANCY AND NEWBORN,

R Krishnaswamy, Y Bakri, P Sasidharan, Department of Pediatrics, King Faisal Specialist Hospital and Research Centre, Riyadh

Malignancy during pregnancy poses a challenge to the clinician in the management of the mother and fetus. In order to ascertain effects of malignancy on pregnancy and the fetus and newborn, we reviewed the charts of 70 mothers who had cancer during pregnancy. They were separated into three groups according to the temporal relationship of cancer to pregnancy. Group I consisted of 37 mothers who had active cancer during pregnancy. Group II consisted of 14 pregnant women who were in remission for two years, and Group III consisted of 19 pregnant women who were in remission for longer than two years. The following variables were analyzed in each group: maternal age, gravida, miscarriage, mode of delivery, live births, gestational age, onset of cancer, mode of therapy, type of cancer—primary and metastatic, outcome, Apgar scores, birth weights, head circumference, ponderal index, and neonatal course. The mean birth weight and gestational age of Group 1 infants were significantly lower than those for Groups II and III. There was no difference between Groups II and III in any of the variables. Further analysis of Group I was carried out with respect to the mode of therapy, treatment versus no treatment, and onset and duration of cancer during pregnancy. Group I mothers had a higher incidence of pregnancy loss due to miscarriage and therapeutic abortion. There was no evidence of intrauterine growth retardation in these groups. Mode of therapy (radiation, chemotherapy, surgery, or a combination) did not influence neonatal outcome. Of the mothers in Group I 62.5% refused treatment and their infants were normal. Thus, our findings indicate that, besides the higher incidence of prematurity, malignancy during pregnancy does not compromise neonatal outcome. Subsequent pregnancies were normal in these women. These data should reassure the clinician in managing malignancy during pregnancy.

CAUSES OF CEREBRAL PALSY IN THE PERINATAL PERIOD, M Leven, Paediatrics and Child Health, The General Infirmary at Leeds, Leeds, England

The prevalence of cerebral palsy (CP) in the Western world is approximately 1 per 1,000 children. It has been shown that probably only 20% of children with CP have a clearly recognized perinatal cause for their condition. These infants can be divided into those born prematurely and those born at full-term. Severe prematurity has a high risk of intracranial hemorrhage (50%) and periventricular prematurity has a high risk of intracranial hemorrhage (50%) and periventricular leukomalacia (12%). A large prospective follow-up study of 200 very-low-birthweight babies showed that hemorrhage confined to the ventricles was a benign condition but cystic periventricular leukomalacia predicted CP with a high degree of accuracy. Cysts involving the occipital region of the brain or those infants in whom cysts were multiple had the worst prognosis. Birth asphyxia is an important cause of CP in full-term babies. One per 1000 full-term infants die or are severely handicapped as a result of this condition. The prediction of CP by means of Apgar score or delay in establishing respiration is very insensitive. The prediction of outcome is more reliably achieved by means of clinical neurological abnormality graded as postasphyxial encephalopathy. If the infant suffers mild encephalopathy which is reversed within 48 hours, the prognosis is excellent. Twenty-five percent of infants with moderate encephalopathy are severely handicapped and 75% of infants with severe encephalopathy are handicapped or die. Postasphyxial encephalopathy is the most accurate method of predicting CP in full-term babies.

THE MANAGEMENT OF BIRTH ASPHYXIA, M Levene, Department of Paediatrics and Child Health, The General Infirmary at Leeds, Leeds, England

Birth asphyxia occurs with an incidence of six per 1000 full-term deliveries. The majority are mild, but 1 per 1000 children or are severely handicapped as a result of asphyxia occurring in the intrapartum period. Management is directed toward minimizing complications and keeping the infant in optimal condition. Any baby with moderate or severe encephalopathy should be nursed in an intensive care environment. Attention should be paid to adequate hydration, avoidance of hypoglycemia and cold stress, and any suspected infection appropriately treated. In particular, there are three complications that are potentially amenable to treatment in severe birth asphyxia: (1) *Hypotension.* Almost half of severely asphyxiated infants have a highly labile blood pressure which on occasion may be sustained at levels below a mean arterial blood pressure of 40. Continuous blood pressure monitoring is necessary to detect this and should be treated with plasma or inotrope support. (2) *Seizures.* Only half of babies with electroconvulsive seizures show abnormal clinical movements. It is not known whether complete suppression of seizures will modify the outcome but this is unlikely. Clinically observed seizures should be treated with phenobarbitone and clonazepam as a second-line anticonvulsant. There is no evidence that it is necessary to abolish all seizures following birth asphyxia. (3) *Brain swelling.* It is widely believed that cerebral edema occurs after birth asphyxia. Approximately two-thirds of babies with severe birth asphyxia develop raised intracranial pressure, but in only a third of these is it possible to treat this successfully with mannitol or other agents. The management of birth asphyxia is largely supportive but the introduction of a variety of new potentially brain protecting drugs allows the possibility that in the future we may have more effective management for this condition.

HYPOMAGNESEMIA IN FULL-TERM INFANTS WITH SEVERE HYPERBILIRUBINEMIA, YK Abu-Osba, GW Imseeh, RW Hann, Neonatology Section, King Faisal Specialist Hospital and Research Centre, Riyadh; Pediatric Department, Dhahran Health Centre

Magnesium is present in the RBC wall, contributing to the maintenance of its integrity and decreasing hemolysis. To investigate the role of hypomagnesemia in severe hyperbilirubinemia secondary to hemolysis, we measured serum magnesium, bilirubin, anbd calcium in all full-term newborns admitted to our NICU with total bilirubin > 19 mg/dl who required exchange transfusion and had G6PD deficiency or blood group incompatibility. Infants of diabetic mothers and small for gestational age infants were excluded. Thirty-one infants met these criteria. Eighteen infants (58%) had G6PD deficiency and 13 (42%) had blood incompatibility. Total bilirubin mean was 24.9 mg/dl (range, 19-40) and indirect bilirubin mean was 22.2 mg/dl (range 16.8-34.8) at mean age of 3.98 days (range, 3-7). Serum magnesium mean was 1.25 mg/dl (range, 0.6-1.9; normal, 1.8-2.4); 23 infants (74%) had magnesium level < 1.5 mg/dl. Serum calcium mean was 9.5 mg/dl (range, 7.7-10; normal, 7.5-11.4); only one infant had hypocalcemia. This high incidence of hypomagnesemia in infants with severe hemolysis and the high incidence of isolated hypomagnesemia without hypocalcemia was not reported. Whether hypomagnesemia increases the susceptibility of RBCs to hemolysis in the presence of other risk factors such as G6PD deficiency or blood incompatibility, or the serum bilirubin interferes with serum magnesium measurement, is not known. This study emphasizes the need to measure serum magnesium in infants with hyperbilirubinemia and raises the question whether magnesium should be supplemented to decrease severe hemolysis.

THE UNUSUAL PHENYLKETONURIAS OF SAUDI ARABIA: PT Ozand, H Hughes, G Gascon, King Faisal Specialist Hospital and Research Centre, Riyadh

We have recently discovered a large number of unusual types of phenylketonuria (PKU) in Saudi Arabia, where the primary defect is the inability to synthesize biopterin. The symptom complex is known as biopterin-dependent PKU (BD PKU). We have seven patients who have BD PKU. While in the West 99% of PKU cases are classic (i.e., they lack the phenylalanine hydroxylase protein), it appears that in the Kingdom the rarer type of the disease (i.e., biopterin-dependent) prevails. In cases of classic PKU the disease is rarely manifested before 1 year of age. In BD PKU, severe hypotonia, failure to thrive, brainstem symptoms, and seizures are manifested as early as 2 months of life. In BD PKU the patient cannot synthesize the neurotransmitters of serotonin, dopamine, and norepinephrine, and is unable to convert phenylalanine to tyrosine. Therefore such patients are more severely affected than in classic PKU. In BD PKU the patient fails to respond to the dietary restriction of phenylalanine, but promptly normalizes the elevated levels of blood phenylalanine after oral administration of the cofactor, tetrahydrobiopterin (BH4). BD PKU is an easily and successfully manageable disease, even when initial diagnosis is delayed. Neurological status improves upon oral administration of BH4 and the neurotransmitter precursors L-5 hydroxytryptophane, dopa, and carbidopa. Since in BD PKU the blood phenylalanine elevation may occur late, neonatal screening may miss the presence of the disease (i.e., be falsely negative). We suggest that, in addition to PKU screening, a neonatal screening procedure for BD PKU must be implemented in the Kingdom.

AUTOIMMUNE THYROIDITIS IN CHILDREN AND ADOLESCENTS: PRESENTATION AND FOLLOW-UP, FM Mousa, EA Mikail, Maternity and Children's Hospital, Riyadh

Thirty cases of autoimmune thyroiditis were seen and followed during the period 1984 to 1988 in the endocrine clinic, Maternity and Children's Hospital, Riyadh. The population included 26 patients and four mothers. Diagnosis was based on the following criteria: (1) presence of thyromegaly (2) thyroid hormonal status (T3, T4, TSH), and (3) presence of significant titers of antithyroglobulin antibodies (ATA) and/or antimicrosomal antibodies (AMA). Twenty-two were females and 4 were males (ratio, 5.5:1). Evaluation of the 26 cases showed: 3 (11.5%) cases had hyperthyroidism; 23 cases were subdivided into three groups: Group A (euthyroid) 8 (30.7%) cases with normal plasma T3, T4, and TSH (normal values: 0.8-1.73 ng/ml; 5-13 μg/dl; 1.5-5 μU/ml, respectively). Group B (compensated hypothyroidism) 5 (19.3%) cases with normal T3, T4, but high TSH more than 10 μU/ml). Group C (overt hypothyroidism) 10 (38.4%) with low T3, T4, but high TSH (25-50 μU/ml). Three of the mothers were euthyroid and one had overt hypothyroidism. L-thyroxine (50-150 μg/day) was given to all patients in Groups B, and C. The three groups were followed for 18 to 30 months (median, 23 months). Clinical and laboratory evaluation was done every 3 to 4 months. Three cases were lost to follow-up, two from Group A and one from Group B). Treatment was withdrawn from patients in Groups B and C when hormonal status reverted to normal. Follow-up for a median of 20 months and a periodic evaluation showed: of the six in Group A, four (20%) remained euthyroid 40 months from the time of initial evaluation, and two (10%) developed hypothyroidism. Three (15%) patients from Group B remained euthyroid and one (5%) patient returned to hypothyroid state. Six (30%) patients from Group C remained euthyroid, while four (20%) patients reverted to hypothyroidism. These data indicate that 13 (65%) patients with autoimmune thyroiditis remained or reverted to euthyroidism after four years of follow-up. More lengthy close observation and evaluation is needed before autoimmune thyroiditis can be considered to have a bright outcome in children and adolescents.

CELIAC DISEASE IN SAUDI CHILDREN, H Nazer, N Sakati, H Harfi, Department of Pediatrics, King Faisal Specialist Hospital and Research Centre, Riyadh

Celiac disease (CD) is a recognized cause of chronic diarrhea and growth retardation in infancy and childhood. Therefore, it presents an important challenge to clinicians, especially those working in developing countries where chronic diarrhea poses a major health hazard. This report confirms the existence of celiac disease in Saudi Arabia and highlights the delay in diagnosis. Twenty-two Saudi children were diagnosed to have CD during 1978 to 1988. They were referred with growth retardation and abdominal distention. History of chronic diarrhea was present in 21 children and recurrent vomiting in 13. Mean age at onset of symptoms was 1.9 years (range, 0.3-11); at referral, 3.4 years (range, 0.4-11.5); and at established diagnosis, 5.9 years (range, 0.9-16), with a mean delay in diagnosis of 2.8 years (range, 0.2-11). Intestinal biopsies were obtained in 21 cases. The remaining patient underwent initial biopsy abroad. Sixteen patients had evidence of severe mucosal injury (flat mucosa) and six patients had partial villous atrophy. Fifteen children responded well to a gluten-free diet (GFD) with relief of diarrhea and abdominal distention and improvement in height, weight, and mood. Intestinal biopsies were obtained from ten children, with evidence of histological remission in seven. Poor compliance to GFD contributed to the lack of favorable response in three children, with evidence of histological relapse in two. Clinical response following gluten challenge was reported in all seven patients studied; three also had histological relapse. It is concluded that the relatively low prevalence of CD in Saudi Arabia may be due to failure of diagnosis. Poor compliance to GFD explains the high rate of nonresponse among children with CD. A higher index of suspicion for the diagnosis of CD in Saudi Arabia is needed.

CORD BLOOD SCREENING FOR THE DETECTION OF RED CELL GENETIC DISORDERS, GA Niazi, H Yaish, JP Dery, M Shaalan, King Fahad National Guard Hospital, Riyadh

The incidence of certain red blood cell genetic disorders has been reported to be high in certain parts of Saudi Arabia, resulting in a major public health problem. Between October 1987 and December 1988, 3924 cord blood samples were screened to determine the incidence of various red cell genetic disorders in newborns delivered at KFH-SANG during this period. Furthermore, a peripheral blood smear was routinely examined for the purpose of correlation and early detection of red blood cell abnormalities which would not be detected otherwise. Eighty-five newborns (65 males, 20 females) were found to be severely G6PD deficient with an overall incidence of 2.2% or a 3.3% incidence among male newborns. The prevalence of the alpha thal gene was found to be 5%, based on a level of Hb Barts (> 1%) and mean corpuscular volume (MCV) < 100 fl. Four cord blood samples have revealed findings consistent with major sickle cell disease; 28 samples were compatible with sickle cell trait (0.7%). Seven samples yielded other abnormal hemoglobins (3 HbE; 1 HbGPhiladelphia; and

3 HbAFX). Four peripheral blood smears revealed bizzare morphologic pictures of the red blood cells, associated with low MCV and mean corpuscular hemoglobin (MCH) and a markedly elevated RDW. Two of the four developed prolonged hyperbilirubinemia, reticulocytosis, and anemia. They were transfusion dependent until several months of age, and presumptive diagnosis of HPP was made pending confirmation by red cell membrane studies. The other two had an uneventful neonatal course even though their morphologic abnormality continues. In view of the relatively high incidence of red cell genetic disorders among Saudi newborns and the tendencey to our population not to attend well baby clinics, cord blood screening will continue to be a valuable diagnostic tool in predicting the clinical course of newborns, thus contributing to a remarkable decrease in the mortality and morbidity of our newborns.

CONGENITAL ADRENAL HYPERPLASIA: NEONATAL SCREENING, ANTENATAL DIAGNOSIS, AND TREATMENT IN UTERO, P Rochiccioli, Department of Paediatrics, Rangueil University Hospital, Toulouse, France

Congenital adrenal hyperplasia is one of the most frequent and one of the most serious endocrine diseases in children. Recent work has led to systematic neonatal screening and also to prenatal diagnosis and fetal treatment of the sexual ambiguity. Neonatal screening was first described in 1977, using measurement of 17-alpha-hydroxyprogesterone (17-OHP) in dried blood eluate. One million tests have been carried out throughout the world, and we now know that the incidence is 1/14,000, there are few false-positives, and the cost of screening is moderate. However, the main problem is the need to obtain the result before two weeks of life, which is not always possible. Two different methods are used in antenatal diagnosis: HLA typing and measurement of 17-OHP in the amniotic fluid. Antenatal diagnosis is possible after HLA typing of the parents and the index case. However, many possibilities of crossing-over exist which then make diagnosis difficult. Measurement of 17-OHP in the amniotic fluid gives a definite diagnosis, as levels in the affected fetus are always above normal. These two methods are therefore complementary and can be used in association. Sexual ambiguity by virilization of the female fetus can be avoided by treatment in utero. Dexamethasone is used at the dose of 1 or 1.5 mg/day. Treatment must start early, in principle before the third or fourth week of pregnancy, and must be continued until the end of pregnancy. Prenatal diagnosis is then based on HLA typing alone. The results of a multicentric study of 33 pregnancies showed that this treatment effictively prevented virilization of the female fetuses, and was well tolerated both by the mothers and the newborns.

PRESENT METHODS OF INVESTIGATION OF GROWTH RETARDATION OF ENDOCRINE ORIGIN, P Rochiccioli, Department of Paediatrics, Rangueil University Hospital, Toulouse, France

The etiologies of growth retardation are many and varied. The nutritional, genetic, and metabolic origins are now classic and the methods of investigation have not changed greatly over the last few years. Conversely, due above all to the use of biosynthetic growth hormone, there has recently been renewed interest in the endocrine causes and in particular growth hormone deficiencies. New methods of investigation have been developed that allow closer analysis of somatotropic deficiencies. These various methods must therefore be compared in order to plan a strategy of investigations of these cases of growth retardation. Pharmacological provocative tests are the most commonly used but are also the most controversial. A large number of tests exist, and the intensity of the response varies greatly according to the test used. Specificity is low because of scattering of the results, and the lower limit of normal is difficult to define. Consequently, the definition of growth hormone deficiency is necessarily arbitrary; total deficiency is defined as a response < 5 ng/ml to two tests and partial deficiency as a response n 10 ng/ml to two tests. The growth factors somatomedin-C/IGF I are still technically difficult to investigate. Results vary widely according to age and also in the same individual. Moreover, there is considerable overlap between the various groups of normal and deficient subjects. The GHRH test simulates the pituitary and therefore indicates the level at which the deficiency exists. The response is positive in over 70% of growth hormone deficiencies, as the hypothalamus is generally involved. This test is thus of limited use in diagnosis. Endogenous growth hormone secretion is studied by sampling at regular intervals during sleep or during the 24-hour period. Physiological growth hormone secretion can be assessed by calculation of the integrated concentration, and also the pulsatile nature of secretion. Pharmacological tests and the study of 24-hour growth hormone secretion often give conflicting results. These various methods allow a more complete approach to growth hormone deficiencies. By using them in association, a new classification of such deficiencies can now be envisaged: several total deficiences, partial deficiencies, dissociated deficiencies, neurosecretory dysfunction, and simple growth retardation with low somatomedin-C levels. Biosynthetic growth hormone can then be used in a more specific manner.

RAPID DIAGNOSIS OF BACTERIAL MENINGITIS BY A NEW ELISA TECHNIQUE, AM Salih, HS Hassan, P Olcen, Department of Paediatrics, Faculty of Medicine, University of Khartoum, Khartoum, Sudan

Early diagnosis of bacterial meningitis influences favorably morbidity and mortality. To evaluate a new ELISA test (Pharmacia meningitis EIA-test) for rapid diagnosis of bacterial meningitis, CSF was systematically collected from 143 children with suspected meningitis encephalitis in Khartoum (April 1985-November 1986). The EIA-test is based on a sandwich enzyme immunoassay principle to detect the antigens of *Hemophilus influenzae*, type b, *Neisseria meningitidis* (groups A, B, C), and *Streptococcus pneumoniae* (25 selected types). The CSF specimens were also examined by three other methods, namely direct microscopy using Gram's stain (DM), routine culturing, and co-agglutination technique (CoA, Phadebact CSF test). A bacterial etiological diagnosis was made in 44 cases, four of which contained organisms other than those tested for by EIA-test or CoA technique. The percentage of positive specimens detected was highest with the EIA-test (82%), followed by CoA (63%), culture (53%), and DM (28%). Pre-treatment with antibiotics was a feature of the population studies: assay of antibiotics in plasma samples taken on admission documented its presence in 46% of cases. The calculated sensitivity of the EIA-test was 86% (CaA = 69%) and specificity 95% (CoA = 97%). The predictive value for a positive test was 81% (CoA = 87%) and for a negative, 96% (CoA = 93%). Adding its technical feasibility to sensitivity and specificity, the EIA-test seems to be well suited for rapid diagnosis of bacterial meningitis.

LACK OF CORRELATION BETWEEN CHROMOSOMAL ANALYSIS AND CLINICAL OUTCOME IN CHILDREN WITH NEWLY DIAGNOSED ACUTE LYMPHOCYTIC LEUKEMIA,

K Sheth, RJ Aur, G Roberts, King Faisal Specialist Hospital and Research Centre, Riyadh

Eighty consecutive patients 6 months to 13 years (median, 5 years) (54 boys, 26 girls) were entered into this study from January 1984 to December 1986. Bone marrow (BM) aspirates from the 80 patients were obtained at diagnosis for chromosomal analyses by G-banding technique after direct and 24-hour culture. Successful studies were obtained in 45 of 80 patients (56%). NN clones were observed in 31/45 patients (68%), AN clones in 14/45 patients (31%), and no AA clones in any of the patients. Two cases yielded translocations: t(11;19) [girl] and t(1;19) [boy]. Chromosomal study failure rate was 35 patients (43%). Modal numbers, deletions, additions, and translocations on initial chromosomal findings using Pearson chi square statistics were correlated with remission induction failure (including deaths), continuous complete remission (CCR), relapse, and elective cessation of therapy. The correlation for continuity in 2 × 2 tables failed to indicate statistical significance in all parameters studied ($P < 0.3$). Current clinical outcome of the 80 patients is: three refused treatment very early, nine died during RI, two failed to attain complete remission, and 66 attained complete remission. Of these patients, five abandoned treatment in CCR, one died of sepsis in CCR (12 mo), and 22 relapsed during maintenance treatment. Of the remaining 38 patients, 31 were taken off treatment effectively after two years in CCR, one relapsed in BM eight months after stopping treatment, 30 remain in CCR off treatment 24-52 months; (median, 20), and seven remain in CCR on maintenance treatment. Therefore, a total of 37 patients are in CCR. The results obtained in this series failed to demonstrate the importance of chromosomal determination at diagnosis as an index for predicting outcome.

IMPROVED VENTILATION OF INFANTS WITH SEVERE RESPIRATORY DISTRESS SYNDROME UTILIZING LOW-VOLUME/CONDENSATE-FREE VENTILATOR TUBING,

A Abu-Taleb, Altonaer Kinder Klinik, Hamburg, West Germany

Based on the experimental data of Eriksson, Sedin showed the efficacy of high-frequency ventilation (HFV) using short tubing in neonates with severe respiratory distress syndrome (RDS). The benefits of HFV (60-100/min) have been well documented, however, the effects of short ventilator tubing have not been demonstrated. Our technique of utilizing high frequency oscillatory ventilation (HFOV) in conjunction with conventional ventilation required the use of low-volume/low-compliance tubing for the ventilator circuit. Using this ventilator setup we discovered that the use of low-volume/low-compliance tubing by itself, without HFOV, resulted in a significant reduction of ventilation parameters, thereby reducing the need of HFOV. This method of ventilation was used during the past two years in 31 infants with severe respiratory failure. In the beginning we had problems with excessive condensation in the ventilator tubing. Therefore a system was devised to minimize the condensation in the tubing and at the same time maintain 85% humidity at 36.5°C. Our objectives were to improve the ventilatory efficiency of conventional ventilators, hence minimizing the need for HFOV, and to reduce condensation in ventilator tubing while maintaining humidity and temperature of inspired gases. The patient population consisted of 31 neonates, of whom 18 had severe RDS and 13 had respiratory failure due to various other causes. Of the 18 patients who survived, we documented significant improvements in the ventilatory parameters utilizing our technique. At the same time we were able to deliver the oxygen/air mixture at the desired temperature and humidity without condensation in the tubing. We conclude that utilizing our technique of ventilation, we were able to reduce morbidity associated with severe RDS and problems related to condensation in ventilator tubing.

COMPLEMENT-FIXING MEASLES ANTIBODY STATUS IN 9-MONTH OLD SAUDI INFANTS PRIOR TO VACCINATION,

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Measles is still endemic in Saudi Arabia and has been frequently reported in early infancy. Hence a pilot study was undertaken to assess the immune status of children prior to their first dose of measles vaccine. The current recommended age for measles vaccination in Saudi Arabia is 9 months. These infants are reimmunized at 15 months of age for lasting immunity. Children attending the well baby clinic at King Fahd Hospital of the University, Al-Khobar, were screened for measles antibody after informed parental consent was obtained. Serum obtained prior to the first dose of measles vaccine was stored at -4°C until all specimens were available for simultaneous testing. Of 114 children tested for complement-fixing measles antibody, 77 infants (67.5%) were found to have antibody in varying titers. Only 37 infants (32.5%) were still susceptible at the time of immunization. Hence the rationale of using vaccine at a lower age than the currently recommended 9 months will be critically analyzed in our presentation.

HYPERBILIRUBINEMIA IN UNCHALLENGED G6PD DEFICIENCY IN THE NEWBORN,

H Yaish, G Niazi, M Shaalan, GS Ahmed, S Khan, A Abu-Taleb, King Fahad National Guard Hospital, Riyadh

Between October 1987 and December 1988, 3924 cord blood specimens were screened at King Fahad National Guard Hospital for the presence of RBC genetic disorders. Eighty-five newborns (65 M, 20 F), for an overall incidence of 2.2% (3.3% of males), were found to be severely G6PD deficient with values ranging from 0 to 83 mu/10 RBC (mean, 28 ± 40) (N = 210 ± 90). Daily bilirubin level was obtained in all healthy newborns who looked clinically jaundiced, until they reached a level when intervention was deemed necessary or a downward trend was noted. Values higher than normal for any of the first seven days of life were defined as hyperbilirubinemia. Twenty-nine of 85 (36%) G6PD-deficient newborns met the criteria; their peak bilirubin level ranged from 9.7 to 27 mg/dl (mean, 15.6 mg/dl) compared to 8 of 85 (9%) G6PD-sufficient control newborns matched for gestational age, weight, and sex, who also met the hyperbilirubinemia criteria. The peak bilirubin level in this group ranged from 7.5 to 16.5 mg/dl (mean, 12.9 mg/dl). None of the control group required exchange transfusion compared to two newborns in the G6PD-deficient group. Blood group A or B was encountered in 4 of 8 jaundiced newborns in the control group who were born to group O mothers, compared to only 1 of 29 with similar setup in the deficient group. None had a positive Coomb's test. Our study reveals an incidence of hyperbilirubinemia that is significantly higher among G6PD-deficient newborns than in the control group (36% versus 9.0%). Even though several studies have reported such an association, others have failed to confirm it. We also found that 75% of all normal newborns who developed hyperbilirubinemia were also G6PD deficient. Almost all our deficient newborns who developed jaundice did so during the first week of life. Five of 29 had to be readmitted after discharge. One required exchange transfusion. This incidence emphasizes the need for early diagnosis and hence close surveillance in order to avoid morbidity and mortality in this group of newborns.

RICKETS IN RIYADH, H Salman, A Abanay, Suleimania Children's Hospital, Riyadh

Although it is sunny in Riyadh most of the year without significant variation between summer and winter, vitamin D rickets is not rare. Different factors, mainly nutritional (prolonged breast feeding without diversified nutrition, maternal vitamin D deficiency) and social (minimal sun exposure, rapid urbanization), explain this phenomenon. We present 500 cases of rickets diagnosed and screened in Suleimania Children's Hospital over three years. The different clinical presentation at onset was considered, along with the different clinical forms, especially the precocious forms in the first three months of life, the causes (mainly nutritional), and the investigations—classic and more specialized, such as 25 hydroxy D_3 and 1.25 Dihydroxy D_3 levels. We stress the importance of rickets screening in breastfed infants, the importance of rickets prophylaxis from the first weeks of life for breastfed babies, and during the last of pregnancy and lactation for the mothers.

LEAD POISONING AMONG SAUDI CHILDREN: A MAJOR PUBLIC HEALTH HAZARD?, HM Yaish, A Al-Soby, King Fahad National Guard Hospital, Riyadh

In the four-year period 1984 to 1988, we encountered 22 children with evidence of lead poisoning (Pb) at KFNGH in Riyadh. Ten of the children (six males, four females) presented acutely with manifestations of Pb encephalopathy. A presumptive diagnosis of PB poisoning was made retrospectively in the remaining 12 children who were probably overlooked at the time of presentation. The criteria for such diagnosis in this second group is presented. The ages of children with acute presentation ranged from six to 48 months (mean, 18 months). Anemia, vomiting, and seizures were uniformly found in all. High Pb level (53-273 μg/dl) and free erythrocyte protoporphyrin (FEP) (508-2693 μg/dl) were recorded in all. Coarse basophilic stippling was observed in nine of ten children, but all showed marked anisocytosis with elevated RDW. Radiologic evidence of Pb lines in the long bones was found in six of ten and active rickets in three of ten. One case had a moderate rise in the uric acid level. The six infants who had lumbar puncture showed moderate elevation of their CSF protein without pleocytosis. Teething powder was the source of Pb in nine of ten and inhalation of Pb-containing fumes in one patient. All but two survived and one of the survivors developed neurological deficit. Our study, together with the locally published work over the last eight years, suggests that Pb poisoning has been and continues to be a public health threat to the children of some communities in the Kingdom. It also shows that we are probably overlooking some of the children who carry a high level of Pb and who will continue to be overlooked unless a high index of suspicion is maintained. Preventive measures, including intense education campaigns, screening of population at risk, possible legislation to make Pb poisoning reportable, and banning the use of incriminating agents are necessary.

CONGENITAL TALIPES EQUINOVARUS: REVIEW OF 269 FEET IN 187 PATIENTS, AA Youssef, King Fahad National Guard Hospital, Riyadh

The aim of this communication was to stress the importance of managing clubfeet immediately after birth. One hundred eighty-seven patients with 269 clubfoot deformities were analyzed, with a follow-up period of 14 years (105 unilateral and 82 bilateral). The deformity was mild in 49, moderate in 80, and severe in 140. In 125 feet, conservative treatment was started early by repeated manipulations and adhesive strapping. The resistant feet were treated surgically: posterior release in 46 feet, soft tissue release in 80, tibialis anterior transfer in four, Evan's in six, Dwyer's osteotomy in six, Reed's rotational osteotomy of the tibia in one, and Z-plasty in one. The complications of treatment are: fracture of the lower tibial metaphysis, four; plaster of Paris sores, five; plaster dermatitis, 25; rocker bottom foot, six; sloughing of wound edges, 16; contracted medial scar, one; and relapse, 34. One hundred and forty-eight patients with 211 foot disorders came for final assessment and the result was good in 177 cases. In 34 feet, relapse occurred and surgery was repeated in 12. In 22, residual varus was acceptable and compatible with good function. The treatment of clubfoot is still a challenge, but there is a plea for early surgical correction in resistant feet, and we do not hesitate to resort to surgery as early as four to six weeks. Repeated manipulations and adhesive strapping yield the best results in the conservative treatment of clubfoot.

Poster Presentations

HOW SAFE IS CARDIAC CATHETERIZATION IN CHILDREN?, O Galal, King Faisal Specialist Hospital and Research Centre, Riyadh

Before using an invasive procedure, it is recommended that its usefulness be weighed against its possible risks. For this reason, we retrospectively reviewed the data on 1152 heart catheterizations done between January 1982 and March 1988 with regard to risks and problems arising during or after the procedure. The largest number of heart catheterizations performed in one year was 254 in 1984 and the smallest number was 119 in 1987; 94 of the children studied (8.2%) were younger than one month and 77 of them were below two weeks of age; 211 were one month to one year (18.3%) and 847 were older than one year (73.5%). In two children, the bladder was inadvertently punctured but there were no complications. In one other case, catheterization had to be stopped due to uncontrollable bleeding. Twenty-five patients developed bradycardia during catheterization, which had to be treated with drugs; seven patients had asystole, two of whom could not be resuscitated. A total of 1495 angiograms were done (mean, 1.3 per catheterization). Twenty-two angiograms resulted in intramural injection without further sequelae. Balloon atrioseptostomy was performed in 21 neonates. One case only resulted in rupture of the balloon without further complication. The overall fatality within 24 hours after the procedure was 0.5%. In the group of newborns below the age of two weeks the fatality was 6.5% (5/77). Beyond that age, only one death occurred out of 1075 catheterizations (0.09%). These results suggest that the risk of catheterization is small nowadays, but still significant within the first two weeks.

SYMPTOM-FREE INTERVALS IN SICKLERS: DOES PNEUMOCOCCAL VACCINATION HAVE A ROLE?, MAF El-Hazmi, MA Babiker, H Bahakim, AM Al-Sowailem, AS Warsy, King Saud University and Riyadh Central Hospital, Riyadh

To investigate the possible effects of pneumococcal vaccination on the progress of sickle cell disease, two groups of sickle cell disease patients presenting with severe clinical manifestations of the disease were selected as cohorts. One group was vaccinated with the polyvalent pneumococcal vaccine while the other group was not given the vaccine. Clinical manifestations, frequency of painful and infective crises, blood transfusion requirements, hematological parameters, differential counts, and types of organisms encountered were recorded for a period of up to two years for the patients in the two groups. The severity index of the sickle cell disease was calculated for each patient. The overall severity indexes in the two groups were compared and the statistical significance of the findings determined. The results showed lower frequencies of painful and infective crises in the vaccinated patients compared to the nonvaccinated ones. Whether vaccination increases crisis-free interval or not was discussed. Patients with sickle cell disease require supportive and prolonged care that causes a continuous strain on medical resources.

SCREENING FOR CONGENITAL HYPOTHYROIDISM AMONG SAUDI NEWBORNS: PRELIMINARY RESULTS FROM A CENTRAL PROVINCE SCREENING PROGRAM, DI Fattah, JE Beecham, GS Ahmed, J Ellis, King Fahad National Guard Hospital, Riyadh

Screening programs to detect congenital hypothyroidism have been utilized in Western countries for several years based on the premise that early treatment will prevent serious sequela such as mental retardation. To assure success, the method of timing of obtaining the sample should be tailored to the culture. In Saudi Arabia, results reported at a recent endocrinology symposium from an Eastern Province hospital screening program utilizing cord blood samples indicated an incidence of congenital hypothyroidism, approximating one per 4,000 live births among Saudi newborns. We report here preliminary results from a Central Province screening program. Among 8,000 Saudi newborns screened, no cases of true congenital hypothyroidism were detected; two cases of transient hypothyroidism were found. A brief discussion of methodology and experience with the system of screening are presented.

HEMOGLOBIN H DISEASE IN THE NEWBORN: PRESENTATION AND MANAGEMENT, YK Abu-Osba, A Mallouh, RW Hann, Neonatology Section, King Faisal Specialist Hospital and Research Centre, Riyadh, and Pediatric Department, Dhahran Health Center, Dhahran

Hemoglobin H disease is a rare genetic disease in Saudi Arabia, as well as in the rest of the world. Sixteen newborns with Hgb H disease were discovered through cord blood screening for abnormal hemoglobins in about 35,000 Saudi newborns screened at Dhahran Health Centre in the Eastern Province, an incidence of 46/100,000 newborns. Hgb H was confirmed by quantitative hemoglobin electrophoresis and Hgb H stain. Eight infants (two females and six males) were symptomatic in the neonatal period which required intervention. The mean birth weight was 2678 gm (2270-3100); two were small for gestation. Apgar score means and ranges were 6 (4-9) and 7.6 (2-9) at one and five minutes, respectively. Three required resuscitation and two had mechanical ventilation. Hepatomegaly was present in four infants and three had cardiomegaly. Five infants had respiratory distress. Whole blood exchange or RBC transfusion was performed in five infants. Peripheral blood smear was abnormal in all infants. In conclusion, infants with Hgb H disease may present with serious problems in the neonatal period which require intervention. Screening all newborns in areas at risk is indicated and long-term follow-up is needed.

DIDMOAD SYNDROME IN SUDANESE CHILDREN, MAM Salih, T Tuvemo, Department of Paediatrics and Child Health, Faculty of Medicine, University of Khartoum, Sudan

Four Sudanese children developed diabetes insipidus (DI), diabetes mellitus (DM), optic atrophy (OA), and deafness (D)—the DIDMOAD syndrome. They were two boys (aged 15 and 16 years) in one family and a boy and a girl (aged 16 and 3 years, respectively) in another family. The disease had an autosomal recessive mode of inheritance. Diabetes mellitus was the first to appear (at 3 to 8 years) followed by deafness and visual failure, and the disease ended fatally in one patient (aged 20 years). In the other three, diabetes insipidus was confirmed using the water deprivation test for 8 hours. The maximum urine osmolality ranged between 131 to 523 mOsm/kg whereas the corresponding plasma osmolality ranged between 315 to 332 mOsm/kg. Improvement in urine concentrating ability was observed in the three patients following the use of desmopressin (DDAVP, 20 ug intranasally), followed by five hours of dehydration. Intravenous urography, voiding cystourethrography, and ultrasound revealed as well several bilateral hydronephrosis, dilated ureters, and distended bladder without vesicoureteric reflux in all of the three patients. With the high rate of consanguinity prevalent in the region, we reccomend examining children who present with diabetes mellitus for features of DIDMOAD syndrome.

MANAGEMENT OUTCOME OF SYMPTOMATIC PATENT DUCTUS ARTERIOSUS IN VERY-LOW-BIRTH-WEIGHT INFANTS, P Sasidharan, R Heimler, Medical College of Wisconsin, Milwaukee, Wisconsin, U.S.A.

In order to evaluate the outcome of infants with symptomatic patent ductus arteriosus (SPDA) managed medically versus surgically, we retrospectively analyzed the charts of 21 infants who developed SPDA (birth weight, 841 ± 210 gm). Infants were placed into four groups, depending on their management, to fluid restriction, indomethacin, indomethacin + ligation, or ligation only. Our findings indicate that infants who responded to indomethacin had higher birth weights than those who required ligation ($P < 0.05$). Infants who required ligation after indomethacin or without indomethacin had lower birth weights and increased morbidity, 02 days, ventilator days, and hospital days compared to infants treated nonsurgically ($P < 0.05$). Our data indicate that infants of less than 700 gm birth weight require ligation if they develop SPDA and the increased morbidity is partly associated with surgery. Multiple regression correlation analysis of the day of closure of the ductus to birth weights, 02 days, and ventilator days revealed no significant correlation to 02 days and ventilator days, indicating no effect on morbidity. Furthermore, our findings indicate that 75% of infants with severe respiratory distress syndrome develop SPDA and there is a strong association of lung maturation and the presence of patent ductus arteriosus. All infants with respiratory distress syndrome developed bronchopulmonary dysplasia in spite of early closure in the indomethacin group.

SURGICAL MANAGEMENT OF CONGENITAL DILATATION OF THE BILE DUCT (CHOLEDOCHAL CYST), Z Skef, Security Forces Hospital, Riyadh

Choledochal cysts are generally considered to be congenital in origin. This cyst can result in cholangitis or biliary cirrhosis and can increase the risk of biliary carcinoma. Several theories have been considered in its formation and etiology. None have been able to explain all aspects of this entity. It is a rare but correctable disease, especially if discovered early before the occurrence of permanent liver damage. It occurs in 1/200,000 live births in the Western World but is more common in Orientals. The incidence in Saudi Arabia is unknown but rare, this being the only case reported in our hospital records for the last five years, with average deliveries of 3,000 live births per year. Because of its various disadvantages, cystenterostomy has been replaced by hepaticoenterostomy after removal of the diseased bile ducts, with blocking the communication with the pancreatic ducts. We describe an unusual presentation of a child with choledochal cyst, with a successful outcome and review of the recent literature.

MANAGEMENT OF NEGLECTED CONGENITAL DYSPLASIA OF THE HIP: REVIEW OF 62 CASES IN 56 PATIENTS, A Yousef, Department of Surgery, King Fahad National Guard Hospital, Riyadh

I present our experience in the management of 62 cases of neglected congenital dysplasia of the hip in 56 patients 2 to 6 years of age, with a follow-up from 2 to 10 years. Our plan of management was consistent in all cases. A 4-week period of traction, sometimes preceded by subcutaneous adductor tenotomy, was followed by open reduction. Prior to open reduction, a trial of gentle reposition of the hips under a general anesthetic was a failure. Six weeks after open reduction, a derotation varus osteotomy was always performed to correct the anteversion of the neck. The plaster spica is removed after 6 weeks and mobilization of the hips is done in hospital for 2 to 3 weeks before discharge. In open reduction, both heads of the rectus-femoris are cut and tenotomy of the ileopsoas tendon is performed. The obstacles for reduction are: inverted limbus, tight transverse acetabular ligament, and enlarged pad of fat. After excision of the limbus and transverse acetabular ligament, reduction of the hip is always easy. Wedge resection of the capsule is performed and the hip fixed in the most stable position of reduction in mild hip flexion, moderate abduction, and internal rotation (30-90 degrees). Derotation osteotomy is an excellent operation for correction of anteversion of the femoral neck and is almost always followed by good acetabular development. Primary bilateral innominate osteotomy was performed in two hips (in one patient) at the time of open reduction at the age of 2 years. I think most hips do well by derotation osteotomy, and innominate osteotomy was not needed in all our cases treated by derotation osteotomy following open reduction. The result was good in 58 hips and epiphysitis occurred in 4 hips.

CONTRIBUTIONS OF ARAB AND MUSLIM OCULISTS, MZ Wafai, King Khaled Eye Specialist Hospital, Riyadh

Between the seventh and fourteenth century, A.D., 39 separate books were written by 25 authors dealing with eye diseases and their medical and surgical management. Professor J. Hirschberg has listed most of those books, with references to their locations in different libraries around the world. The books from which new ideas originated were discussed and slides presented.

POSTERIOR URETHRAL VALVES: AN OVERVIEW, S Basata, Department of Surgery, King Fahad National Guard Hospital, Riyadh

Congenital posterior urethral valves and related urinary system disorders are pediatric urological problems of great importance, known to all pediatricians and urologists. In some cases, medical care providers of adult patients have to deal with these problems as well. This overview will discuss various topics related to posterior urethral valves with special emphasis on early detection and intervention, including various management modalities and strategies.

SIXTH ANNUAL NEUROSCIENCES SYMPOSIUM

Sponsored by the Joint Board for Postgraduate Education
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SUBARACHNOID HEMORRHAGE IN SAUDI ARABIA, A Ammar, S Al-Rajeh, AW Ibrahim, UM Chowdhary, A Al-Awada, A Shatla, King Faisal University, Dammam

Eighty-two patients with subarachnoid hemorrhage (SAH) were admitted to King Fahd University Hospital, Al-Khobar, Saudi Arabia, between 1982 and 1988, representing 0.1% of the total admissions to this hospital. This hospital serves an estimated 500,000 persons. 76.8% were males and 23.2% were females. 12.2% were under the age of 20 years, 45.1% were between 20 and 40 years, and 42.7% were over 40 years of age. SAH due to ruptured aneurysm constituted 25.6% of the cases, while 14.6% were due to arteriovenous malformation. 11% of the SAH cases were either due to sclerotic changes, blood disease, or moyamoya. In 18% of the cases, the angiogram failed to show the cause of the bleeding. In 30.4% of the cases, angiography was not performed due to poor condition of the patient or rapid death. There is great difficulty in obtaining accurate statistics about the incidence of SAH in the Middle East because of (1) the absence of postmortem autopsy; (2) lack of awareness on the part of the medical staff to the condition due to the false belief that SAH is very rare in the Middle East, and hence, underreporting to neurosurgical centers; and (3) the rapid changes in the structure of the society.

GENETIC ASPECTS OF EPILEPSY WITH IMPULSIVE PETITE MAL (JUVENILE MYOCLONIC EPILEPSY) IN A LARGE FAMILY, M Atassi, Riyadh Central Hospital; G Gason, King Faisal Specialist Hospital and Research Centre, Riyadh

Epilepsy with impulsive petit mal was first described in 1957 by Janz and Christian and was considered a separate entity. In the English-speaking literature it was referred to as juvenile myoclonus epilepsy (JME); however, in previous reports (T. Obeid and C. P. Panayiotopoulos), JME was found to be common in Saudi Arabia, with a high positive family history clearly associated with the marital ritus and consanguinity seen in Arabic countries. A large family was described in which many members showed symptoms typical of JME. Only siblings of consanguineous partners were affected. There was also a high rate of other genetic disorders.

EXPERIENCE WITH STEREOTAXIC SURGERY AT RIYADH ARMED FORCES HOSPITAL, N Amiri, K Al-Moutaery, U Miola, H. Sharif, Riyadh Armed Forces Hospital

Stereotaxic surgery is a well-established procedure worldwide. Nowadays it plays an important role in tumor biopsy, cyst and hematoma evacuation, stereotaxic-guided surgery, and isotope implantation. Our experience with stereotaxic surgery includes tumor biopsy in deep-seated tumors and in lesions where we suspect an infectious origin (e.g., tuberculosis). All cases were performed under general anesthesia. The coordinates of the target, x,y,z, were measured by CT scan. There was no mortality or morbidity.

CLINICAL EXPERIENCE IN MAGNETIC STIMULATION, SA Bohlega, King Faisal Specialist Hospital and Research Centre, Riyadh; A Eisen, University of British Columbia, Vancouver, Canada

Magnetic stimulation opens a new horizon in studying central motor conduction. Using a DENTAC II magnetic coil, motor evoked potentials (MEP) were elicited in 123 subjects (50 controls, 73 patients). Significant side effects were not encountered. Normal thenar MEP measured 19.9 ± 1.6 msec; tibialis anterior, 27.2 ± 2.9; and biceps, 12.6 ± 2.4. The thenar latency correlated within arm's length but the tibialis anterior latency did not correlate with light. Central motor conduction time between the motor cortex and C7 and between the cortex and L5 measured 5.4 ± 1.7 msec and 12.1 ± 3.8 msec, respectively. Spinal cord conduction velocity measured 63 m/sec. Normal thenar MEP amplitude exceeded 20% of the maximum thenar m wave. 50% of patients with multiple sclerosis and 45% of patients with amyotrophic lateral sclerosis had abnormal MEPs while patients with Huntington's and Parkinson's diseases had normal thenar MEPs.

STROKE IN PATIENTS WITH ATRIAL FIBRILLATION: A RETROSPECTIVE STUDY OF 169 CASES, W Chalak, MZ Khawajeh, M Rifaat, V Sivanandam, MG Garg, MA Araoye, M Atassi, H Dawood, NA Pirzadah, AG Al-Akeel, Department of Medicine, Riyadh Central Hospital

Over a period of three years (1.6.1405-1.6.1408), 169 patients were hospitalized at the Riyadh Central Hospital because of atrial fibrillation and stroke. The sex distribution was even, with males 52% and females 48%. Mean age was 65 years, ranging between 13 and 110 years. We observed a slight predominance of permanent atrial fibrillation compared to the paroxysmal type—56.9% versus 43.2%, respectively. The main causes were myocardial infarction, 20%; chronic ischemic heart disease without myocardial infarction, 39%; mitral stenosis, 12%; hypertensive heart disease, 9.5%; and lone atrial fibrillation, 9.5%. The heart was decompensated in 15% of the cases, and 25% of the patients were hypertensive. Of these patients, 35% had one or more brain infarctions and in 10% it was a hemorrhage. Mortality was 50%.

INFANTILE SPASMS AT RIYADH ARMED FORCES HOSPITAL, N Biary, VA Nottidge, SM Al-Deeb, Riyadh Armed Forces Hospital

Eighteen patients (9 boys, 9 girls) with infantile spasms (IS) were identified within the past 30 months at Riyadh Armed Forces Hospital. Age at onset of IS was between 1 and 19 months. Hypsarrhythmic EEG patterns were seen in patients aged 6 weeks to 4 years. Multifocal sharp waves were seen at the age of 1 month. Seven girls had agenesis of the corpus callosum. Six patients had cerebral atrophy on CT scan or MRI. One had tuberous sclerosis. One patient developed IS at the age of 19 months associated with a cerebral hemorrhage secondary to skull fracture. Other causes included toxoplasmosis, left cerebral infarction, and postencephalitis. Treatment included ACTH, dexamethasone, valproate, and clonazepam. It is concluded that the occurrence of agenesis of the corpus callosum in IS is high; one of our patients had idiopathic hypsarrhythmia, and clear hypsarrhythmic EEG patterns were identified at the age of six weeks.

PAPILLEDEMA SECONDARY TO CEREBRAL VEIN THROMBOSIS VERSUS PSEUDOTUMOR CEREBRI (BIH), PS Chavis, M Badr, King Khaled Eye Specialist Hospital; MZ Al-Kawi, King Faisal Specialist Hospital and Research Centre, Riyadh

Twenty-eight patients with benign intracranial hypertension were evaluated with neurological examination, CT scan, and lumbar puncture; six patients had cerebral vein thrombosis documented on digital subtraction angiography. The cerebral vein thrombosis was secondary to definite Behcet's disease in two, possible Behcet's in one, oral contraceptives in one, a coagulopathy in one (with prolonged euglobulin lysis time), and unknown cause in one. The fundus appearance, visual acuity, and vision field in the two groups of patients was contrasted, and pertinent features of the cerebral vein thrombosis group are sufficient to make the diagnosis suspect when one considers the number and location of hemorrhages, cotton wool spots, and changes of the optic papilla. The prognosis for the vein thrombosis group relates initially to prompt treatment before visual loss or other neurological sequelae occur. Fundus clues to ready diagnosis are critical in order to prevent the occurrence of irreversible visual loss and to institute proper treatment. Other parameters peculiar to this group of patients with cerebral vein thrombosis were discussed.

OUR EXPERIENCE IN EEG SPECTRAL ANALYSIS (BRAIN MAPPING) IN HEAD TRAUMA, UM Chowdhary, O Bademosi, AW Ibrahim, S Al-Rajeh, SA Ammar, Departments of Neurosurgery and Neurology, CMMS, King Faisal University, Dammam

Computerized analysis of various forms of brain electrical activity have proved to be valuable in long-term monitoring in intensive care and the quantification of event-related potentials. This approach with the use of multichannel spectral analysis has shown that brain mapping is better than routine visual EEG analysis in the assessment of cerebral ischemia. Clinical evaluation of head trauma using the Glasgow Coma Scale (GCS) coupled with CT brain scan to determine structural damage are the cornerstones of evaluation. Spectral EEG analysis is a neurophysiological investigation that may prove useful in evaluating brain function following head trauma. Based on the above premise, we performed brain mapping on 16 patients with different severity of head trauma. All patients had clinical evaluation and underwent standard treatment for their injury. CT brain scan and brain mapping were performed within 24 hours of injury, 72 hours after injury, and one week after injury. The details of our methodology for evaluation of CT scan and for the analysis of brain mapping were presented. We then correlated the GCS and structural damage seen on CT brain scan to the changes shown on brain mapping. The wave patterns of EEG recorded are converted to maps which have been analyzed for frequency, amplitude, and spectral configurations by the computer software. The distribution of electrophysiological disturbances as shown by the spectral analysis has been correlated to GCS and the traumatic cerebral parenchymal lesion. Similar correlation was done among these factors during the recovery phase of the head-injured patient. We found a very good correlation in the location of the spectral abnormality and the structural damage. During recovery phase the spectral abnormality improved earlier than the structural damage. We describe our methodology, the technical parameters, and details of the correlation achieved between GCS, spectral analysis, and structural cerebral damage.

CEREBRAL VENOUS THROMBOSIS, AK Daif, T Obeid, S Al-Deeb, AR Shamena, B Yaqub, King Khalid University Hospital and Riyadh Armed Forces Hospital, Riyadh

Cerebral venous thrombosis (CVT) is a rare condition with diverse manifestations that may be the result of a variety of pathological processes. We presented 14 adult cases from King Khalid University Hospital and Riyadh Armed Forces Hospital discovered during that last 4 years. The most frequent symptoms and signs were headaches which occurred in all 14 patients (100%) and papilledema found in 12 cases (85%). Among the focal deficits, the most common were: two patients with hemiplegia (14%) and three patients with multiple cranial nerve palsies (12%). Associated conditions and possible etiologies were: 16 patients with neuro-Behcet's syndrome (42%), two with malignancy, one with systemic lupus erythematosus, two with coagulation disorders, one on oral contraceptive steroids, and two with idiopathic cases. CT scans of the brain were abnormal in six patients (42%), while digital subtraction angiography and medical resonance imaging were abnormal in those patients who had these investigations. Our study showed that CVT was not uncommon in Saudi Arabia and neuro-Behcet's syndrome is the most common identifiable cause among our patients.

BRUCELLOSIS AND THE NERVOUS SYSTEM, S Al-Deeb, B Yaqub, H Sharif, Neurology Units at Riyadh Armed Forces Hospital and King Khalid University Hospital, Riyadh

We have evaluated 37 patients with neurological deficit due to proven active brucellosis who were treated in two main hospitals in Riyadh. Twelve patients had myelopathy or root lesions due to compression from vertebral lesions or extradural granulomas. The remaining 25 patients had neurobrucellosis and were categorized into five groups: (1) meningoencephalitis (nine patients); (2) papilledema without lateralizing features (four patients); (3) meningovascular: three patients presented with transient ischemic attacks or hemiparesis; (4) CNS demyelination: three patients presented with subacute disseminated encephalomyelitis and ataxic quadriparesis; and (5) five patients had peripheral neuropathy, L5 root lesion, cranial nerve mononeuritis, and polyradiculitis. The CSF was abnormal in all patients and showed high protein, low or normal glucose, and lymphocytic pleocytosis. CSF (and blood) *Brucella* IgG agglutination titers were significantly raised in all patients, while *Brucella* organisms were isolated from the CSF in only 60% of the patients. IgG oligoclonal bands were done in ten patients and were detected in the blood and CSF in nine. CT and MRI findings were consistent with brain edema, in meningovascular and extensive white matter lesions in CNS demyelination. The neurophysiological studies in the polyradiculitis cases were consistent with peripheral demyelination. Patients with meningoencephalitis, papilledema, and meningovascular lesions recovered completely, while those with central or peripheral demyelination had incomplete recovery.

LUMBAR CANAL STENOSIS IN SAUDI POPULATION, H Elminiawi, P Iqbal, Dammam Central Hospital, Dammam

Lumbar canal stenosis is a relatively common problem in Saudi Arabia. Between September 1983 to September 1988, 63 patients needed surgical treatment of a documented narrow lumbar canal. (This represents about 25% of all operations performed in the lumbar region during the same period.) To determine the normal size of the spinal canal in the Saudi population, 50 normal Saudi citizens were examined with the CT scanner, none of whom had any back or leg pain. This report summarizes our clinical experience with these patients, including the types of stenosis (etiology), clinical presentation, neurological findings, radiological findings, surgical management, and outcome. We also presented the most important parameter in 50 normal Saudi citizens from L1 to L5.

SAUDI LEUKODYSTROPHY: A NEW ENTITY?, GG Gascon, PT Ozand, Department of Pediatrics, King Faisal Specialist Hospital and Research Centre, Riyadh

In 26 patients with leukodystrophy seen between 1986 to 1988, we were unable to make a definite diagnosis in 22. All presented in early or late infancy with deterioration in motor development, long tract pyramidal signs, varying degrees of dementia, and optic atrophy with failing vision. All parents were consanguineous and a few families had multiple siblings involved. Neuroimaging studies revealed diffuse leukoencephalopathy with mild cortical atrophy. CSF protein was normal; visual evoked responses and brainstem auditory evoked responses showed increased latencies. All had normal ACTH stimulation tests as well as urine pipecolic acid and lysosomal enzyme assays. The brain biopsy in one patient was inconclusive and no postmortem examinations were done. Our suspicion was that this group fell into the classification of sudanophilic leukodystrophies.

THE TREATMENT OF LUMBAR DISC PROLAPSE BY OUTPATIENT MICRODISCECTOMY, HB Griffith, A Jamjoom, Department of Neurosurgery, Frenchay Hospital, Bristol, England

It is well recognized that the practice of microdiscectomy in the treatment of lumbar disc disease has resulted in decreased postoperative hospital stay. Increasing experience with the procedure has made it possible to offer the operation to patients safely on an outpatient basis. Between 1985 and 1988, 40 patients (28 males and 12 females), age range, 19 to 67 years, underwent day case lumbar microdiscectomy at Frenchay Hospital, Bristol. All patients lived within 15 miles of the hospital and had a person at home to attend to their needs during the first five postoperative days spent in bed. The disc prolapse was at L4/5 in 17 cases, at L5/S1 in 22 cases, and at L3/4 in one case. Diagnosis was confirmed by CT scans in all but two cases in which the diagnosis of an L5/S1 prolapse was based on the clinical picture only. The operation was performed via a 1-cm skin incision under x-ray control for accurate interspace marking. Thirty-six patients returned home on the same day. Four patients were kept in the hospital overnight because of a breach of the dura mater in one case, the exploration of two levels in another, and transport difficulties in two. No patient had problems with postoperative pain or difficulty passing urine. One patient required urgent re-admission 48 hours after operation because of severe backache which abated with bedrest. Six patients had further disc prolapse, necessitating a reexploration over a period from one week to ten months.

THE TREATMENT OF CHILDHOOD HYDROCEPHALUS BY ENDOSCOPIC CHOROID PLEXUS COAGULATION AND POSTOPERATIVE VENTRICULAR PERFUSION WITH ARTIFICIAL CEREBROSPINAL FLUID, HB Griffith, A Jamjoom, Department of Neurosurgery, Frenchay Hospital, Bristol, England

Childhood hydrocephalus is a common disorder that is usually managed by CSF shunting, a procedure which has numerous well-recognized complications. Endoscopic choroid plexus coagulation is a safe alternative treatment, which if successful, provides a permanent cure. In 1986 the author (H.B.G.) published a series of 70 cases of choroid plexus coagulation with the findings that in 49% the hydrocephalus was controlled without a shunt or in the presence of a shunt which proved to be nonfunctional. It is likely that when choroid plexus coagulation does not work it is due to postcoagulation blood and protein released into the CSF, which by interference with the function of the arachnoid villi further damages absorption function. In our current study we attempted to eliminate the latter effect by introducing postoperative perfusion of the ventricular system with artificial CSF. This new technique was performed on 23 cases between 1985 and 1988. The age range of the patients was between one month to five years; 18 patients were aged less than six months. The ventricular perfusion with artificial CSF was carried out at the rate of 40 ml/hr for 36 to 96 hours' duration. All cases were perfused immediately following coagulation. Six patients had separate precoagulation perfusion because their CSF was blood stained. Four patients had repeat postcoagulation perfusion because of increased CSF protein content associated with an enlarging head. A total of 38 perfusions were performed. There were seven cases of meningitis; however, none have occurred since a new double-antibiotic regimen was introduced in the last 13 perfusions. Only nine patients required shunting. In this series, hydrocephalus in 61% of the patients was controlled by choroid plexus coagulation and CSF perfusion.

THE ADVANTAGE OF THE MUSCULOCUTANEOUS FLAP FOR THE REPAIR OF MENINGOMYELOCELE, M Hegazy, A Ammar, AW Ibrahim, UM Chowdhary, Departments of Plastic Surgery and Neurosurgery, King Faisal University, Dammam

The standard method for repairing thoracic-lumbar-sacral meningomyelocele is either adjusting the edges of the skin by rotating the skin flap or releasing the incision. These methods, in spite of their major popularity among neurosurgeons, have well-documented complications such as skin necrosis, infection, and cosmetically unacceptable results. We adopted the use of the reverse latissimus dorsi musculocutaneous flap to overcome these disadvantages. Ten patients with different sizes of thoracic, lumbar, and sacral meningomyelocele were operated on by this technique. None of the patients developed CSF leak or infection postoperatively. In all cases, the wound healed well. A further advantage is also provided by this method in that it does not produce compression of the spinal cord and nerve roots, as occurs with conventional methods of closure.

LOCAL EXPERIENCE WITH NEURAL TUBE DEFECTS IN THE EASTERN PROVINCE, AWM Ibrahim, K Omran, UM Chowdhary, A Ammar, A Dawodu, King Faisal University, Dammam

Children with neural tube defects who were born at or admitted to King Fahd Hospital of the University (KFUH) over a 6-year period (January 1983 to December 1988) were recorded and analyzed. A total of 87 cases were documented. Of these, 53% were females (46 cases) and 47% were males (41 cases), making the male to female ratio 1:1.1. Thirty-six patients (41.3%) were born at KFUH. The total number of deliveries during the study period was 15,788 deliveries, making the frequency of neural tube defects 2.29/1000 live births. Mean maternal age at delivery was 23 years; 68% were Saudis, 24% were Arabs, and the rest were of other nationalities. Consanguinity was observed in 25% of the parents of Saudi children. The average age of the patients referred with neural tube defects from other hospitals was 2.45 days, signifying a considerable delay in the referral. Regarding antenatal care, 22 patients had regular antenatal care, 34 had irregular antenatal attendance, and 31 mothers had no antenatal care. In only one patient was antenatal diagnosis of the neural tube defect made. Twenty percent of the mothers had noticed decreased fetal movement. Two had no antenatal hemorrhage, three had premature delivery, and two had premature rupture of the membranes.

Twelve mothers were illiterate, 13 had elementary education, 23 had a high school education, and 39 had a university education. Previous history of a neural tube defect was observed in two patients only. As for the location of the lesions, 56.3% had myelomeningoceles (44 cases) situated in the lumbar sacral area and five cases had a thoracolumbar lesion. In the 21.8% of patients with encephalocele, the distribution was as follows: 15 occipital, 2 frontal, and 1 nasal. Spina bifida occurred in 9 cases. The frequency of anencephaly is 0.5/1000 live births. Associated anomalies were observed in 44.6% of the cases. Analysis of data and correlation to local regional and international data were further discussed and presented. The relevance of these data in elucidating the frequency and pattern of neural tube defects in this region is an important indicator to the size of this serious problem.

EPILEPSY IN PATIENTS WITH BRAIN TUMOR, M Al-Jaberi, N Biary, SM Al-Deeb, Y Subeiti, N Al-Zahrani, I Koreich, W Khoja, K Moutaery, Riyadh Armed Forces Hospital

Three hundred and fifty patients with brain tumor were reviewed at the Riyadh Armed Forces Hospital; 33% had epilepsy and 9% had epilepsy as a first symptom. The type of epilepsy was partial simple in 21%, partial complex in 10%, and secondary generalized in 69%. 33% required more than one drug. Phenytoin was used in 63% of the cases with a 28% failure; carbamazepine was used in 21% with a 57% failure. The relationship of the tumor, type, grade, and location to epilepsy were discussed.

DIAGNOSTIC ROLE OF EVOKED POTENTIAL AUDIOMETRY AND BRAINSTEM AUDITORY EVOKED POTENTIALS IN NEUROBRUCELLOSIS, MU Kabiraj, AR Shamena, S Al-Deeb, B Yaqub, M Al-Bunyan, AK Daif, A Hussein, King Khalid University Hospital, Riyadh

We analyzed the evoked potential audiometry (EPAs) and brainstem auditory evoked potential (BAEPs) in two groups of patients: Group I–10 patients with systemic brucellosis and nonspecific neurological findings such as headache and myalgia; Group II–10 patients with neurobrucellosis. In Group I, the EPA and BAEPs were normal in all patients. In Group II, EPAs were unilaterally or bilaterally abnormal in all patients, with increased hearing threshold from 40 dB to 95 dB. The BAEP abnormalities were categorized into four types: (1) Absent, delayed, or low amplitude wave I with normal or short I-V interpeak wave latency. These abnormalities were bilateral in three patients with polyradiculitis, myelitis, and ataxic quadriparesis. Serial BAEP studies in two showed no improvement with treatment, indicating irreversible damage to the cochlea or cochlear nerve, probably due to direct invasion of the bacteria or its endotoxin. (2) Normal wave I, but prolonged I-III interpeak wave latency, bilaterally; in three patients with papilledema without lateralizing signs and unilaterally in one patient with myelitis. (3) Absent or abnormal waves IV and V complex unilaterally, in two patients with spastic quadriparesis. These were reversible with therapy in one. (4) Prolongation of the central conduction (I-V interpeak wave latency) bilaterally, in one patient with ataxic quadriparesis. Although these abnormalities are nonspecific and occur in other disease conditions, they are important: to understand the etiopathogenesis; to differentiate them from other granulomatous, viral, or bacterial infections; and also to be used as an early indicator of nervous system involvement in systemic brucellosis.

TRANSORAL APPROACH FOR ANTERIOR CRANIOCERVICAL JUNCTION PATHOLOGY, IN Kanaan, B Rahm, R Coates, A Jallu, A Koht, E Siqueira, King Faisal Specialist Hospital and Research Centre, Riyadh

We describe four patients in whom we utilized a transoral approach for odontoid pathology: congenital malformation (3) and neoplasm (1). All patients were studied extensively with CT-assisted myelography, angiography, and MRI. All three patients with a craniocervical junction (CCJ) malformation underwent second-stage surgery for posterior decompression and fusion. The operative mortality and morbidity were nil. One patient needed transoral reexploration for additional removal of the odontoid. The indications for the transoral approach were reviewed. The guidelines for neuroradiological studies with CT-assisted myelography and MRI were given. Microsurgical technical modifications as well as the need for intraoperative neurophysiological monitoring were discussed.

MOYAMOYA DISEASE IN SAUDI ARABIA, MZ Al-Kawi, G Gascon, A Allen, M Banna, King Faisal Specialist Hospital and Research Centre, Riyadh

Moyamoya disease denotes the angiographic appearance or an unusual affliction of blood vessels in the brain. It was first described in Japan, then in other countries, but has not been reported in Saudi Arabia. We observed two cases, the first in a 30-year-old woman, and the second in a 5-year-old girl suffering from a stroke syndrome at a young age. The child had the usual basal form of the disease, while the adult had the less common vault form and presented with an intraventricular hemorrhage. The importance of recognizing this condition clinically as well as treatment approaches was discussed.

SSEP MONITORING DURING THE MANAGEMENT OF CEREBRAL ANEURYSM, A Koht, I Kanaan, E Siqueria, Departments of Anesthesiology and Neurosurgery, King Faisal Specialist Hospital and Research Centre, Riyadh

Cerebral aneurysms have a high perioperative morbidity and mortality due to several factors such as vasospasm, early operative rupture of the aneurysm, increase in the intracranial pressure, and compression of cerebral arteries. The functional effects of decreased blood flow using somatosensory evoked potentials (SSEPs) have been reported previously [Kidooka M, Nakasu Y, Watanabe K, et al. Monitoring of somatosensory evoked potentials during aneurysm surgery. Surg Neurol 1987;27:69-76]. Relevant changes in the SSEPs include prolonged latency, decreased amplitude, or a prolongation in the central conduction time. A drop in cerebral blood flow (CBF) between 20-15 ml/100 gm/min is associated with a temporary loss, followed by permanent disappearance of the signals when CBF drops below 10 ml/100 gm/min. We reported two cases: a giant internal carotid artery (ICA) aneurysm and A2 aneurysm that needed temporary vessel clipping. SSEPs were tested postoperatively in the ICA aneurysm while these were done preoperatively, intraoperatively, and postoperatively in the A2 branch aneurysm. The first case resulted in a postoperative neurological deficit while the second case was intact. However, because the postoperative SSEP testing showed repeatable signals from the deficit side, aggressive treatment with hyperperfusion and intravascular infusion of nimodipine was instituted and the patient regained neurological function. Our experience with SSEP monitoring in Saudi Arabia in addition to previous experience in Germany and USA was discussed.

MALIGNANT BRAIN TUMORS REFERRED FOR RADIOTHERAPY AT RIYADH ARMED FORCES HOSPITAL, W Khoja, Y Subeiti, M Al-Jaberi, N Biary, O Koreich, K Moutaery, N Zahrani, E Khoja, SM Al-Deeb, Riyadh Armed Forces Hospital

Two hundred and seventy patients with malignant brain tumors were assessed at Riyadh Armed Forces Hospital and referred for radiotherapy; 66% were Saudi nationals. Provinces of referral were analyzed. Patient age ranged between 0.14 to 85.6 years. There were 170 males and 100 females. 70% of the tumors were supratentorial and 30% were infratentorial. 33% of the patients were below the age of 12. Astrocytoma was the most common type of tumor, constituting 41.5%. Medulloblastoma represented 12%, pituitary 10%, and neuroblastoma 9.6% of the tumors. Relationship between age, sex, type, and location of the tumor was discussed.

PATTERNS OF NONSURGICAL MANAGEMENT OF PRIMARY NEUROLOGICAL MALIGNANCIES: THE ARMED FORCES HOSPITAL EXPERIENCE, O Koreich, M Al-Jaberi, N Al-Biary, Y Al-Subeiti, N Al-Zahrani, Riyadh Armed Forces Hospital

Since its commissioning in 1981, the Department of Oncology at the Armed Forces Hospital, Riyadh, has been treating referred cases of malignant disease. During this period, over 270 cases of neurological malignancies were seen, constituting approximately just over 7% of all malignancies seen. The male to female ratio was 1.7:1. Median age for males was 28.9 years, whereas in females it was considerably younger at 19.5 years. Forty percent of the patients had astrocytoma with nearly two thirds of these in the higher grades III and IV. Medulloblastoma accounted for 12% and pituitary adenomas and neuroblastomas accounted for approximately 10% each. Of the total number of malignancies, only four were prolactinoma. Radiation therapy is one of the main lines of management for primary cranial neoplasms. Chemotherapy has a limited role and is mainly used in cases of primary intracranial lymphoma in which one patient has been treated. Recently chemotherapy has been advocated for the management of medulloblastoma. The long-term complications of radiation, particularly in children, who accounted for approximately a third of the patients, include growth abnormalities, hormonal deficiencies, and psychosocial problems. A review of our cases and the literature was presented.

ABDOMINAL EPILEPSY, H Malibary, King Abdulaziz University Hospital, Jeddah

Attacks of abdominal pain can be the manifestation of a special form of epilepsy: the abdominal epilepsy which mainly occurs in children. Eight children, six boys and two girls, were referred to the Neurology Unit of King Abdulaziz University Hospital for evaluation of attacks of abdominal pain. These children were investigated and no local cause could be elicited. The neurological examination was normal but the EEG showed epileptic discharges such as sharp waves, spikes, or polyspikes occurring sometimes in generalized paroxysms. The children were greatly improved under anticonvulsant treatment (phenytoin). The relationship between the nosologic entity and the abdominal migraine was discussed.

THE IMPACT OF MRI ON THE SURGICAL MANAGEMENT OF INFECTIONS OF THE SPINE, K Moutaery, H Sharif, M Al-Wagga, S Al-Deeb, Riyadh Armed Forces Hospital

Patients with spinal infections may present with a wide range of neurological deficits, depending on the degree of associated compression of the thecal sac and/or nerve roots by the infective process, the destroyed vertebrae and disc, and the soft tissue edema. Decisions regarding surgical intervention depend mostly on the progression of the neurological deficit, the level of spinal involvement, and the type of offending organism. The approach for the surgical decompression (e.g., anterior versus posterior) depends on the imaging features of the spinal deformity. Of 53 patients with infective spondylitis (*Brucella* 26, tubercle 23, *Staphylococcus aureus* three, actinomycetes two) seen in this institution in the past 18 months, 15 underwent decompressive surgery, six by the anterior approach (tubercle 14, actinomycetes one). MR imaging was performed on admission for all 53. The presence of an infective etiology was evident on MR in all, and characteristic features were obtained for most of the brucellae and tuberculous infections. In this study, MRI provided adequate information on the level of spinal involvement, the degree of vertebral and disc destruction, the presence or absence of paraspinal soft tissue abnormality, epidural extension, and the severity and nature of associated angulation deformity. Post therapy follow-up was also most conveniently achieved by this modality. We recommend that whenever available, MR imaging should be utilized as the method of first choice for evaluating spinal infections since it provides a summation of most of the data obtained by other modalities (radiography, scintigraphy, and CT).

ATTENTION DEFICIT DISORDERS WITH LANGUAGE DELAY IN SAUDI ARABIA, MJ Nester, King Faisal Specialist Hospital and Research Centre, Riyadh

Attention deficit disorders (ADD) represent a sizable population of high-incidence, low-severity syndromes seen in all areas of the world in which they have been studied, including Saudi Arabia. In spite of their comparatively low severity, they present considerable difficulty in the areas of behavior management and education. Studies have indicated that these are a life-long phenomenon and may have an impact on functioning in the adult as well as the child. Recent studies have indicated the presence of a particular subset of ADD seen in Western countries which links this syndrome with language delay. A series of 18 patients was investigated at King Faisal Specialist Hospital who presented with this combination of symptoms. This subset represents 22% of the total number of patients seen with either a primary or secondary diagnosis of ADD. All patients met the DSM-III-R criteria for ADHD or ADDU. Age range was 3.9 to 14 years, with a mean of 6.69 years. The presence of other factors such as male/female ratio, positive family history, motor delay, school performance, IQ, and response to treatment was addressed. The possibilities for early diagnosis and intervention, particularly involving speech/

language therapy and medication management, were also discussed, along with the potential benefit in respect to school performance. Finally, the need for further research in this area, especially within Saudi Arabia, is mentioned.

PHOTOSENSITIVE EPILEPSY AND PHOTOCONVULSIVE RESPONSES TO PHOTIC STIMULATION IN ARABS, T Obeid, AK Daif, G Waheed, King Khalid University Hospital, Riyadh

Four hundred and thirty epileptic patients were examined clinically and electroencephalographically to determine the proportion with photosensitive epilepsy or showing photoconvulsive response (PCR) to intermittent photic stimulation (IPS). Our preliminary results indicate that photosensitive epilepsy and PCR are not uncommon, especially compared to the rarity of them in Black Africans. This reflects the type of epileptic syndromes and we think that sunshine has little role in influencing inversely the incidence of photoconvulsive response, as suggested previously.

RATIONALE, TECHNIQUE, AND RESULTS OF STEREOTACTIC BRAIN BIOPSY, CB Ostertag, Division of Stereotactic Surgery, Department of Neurosurgery, University of Saarland, Homburg, West Germany

CT-guided stereotactic serial biopsy of brain lesions (1108 cases) is an acceptably safe and accurate procedure that avoids major brain trauma. It offers a logical alternative to craniotomies for lesions of neoplastic, developmental, or infectious origin. The primary objective of stereotactic biopsy is to achieve a morphological as opposed to a radiographic diagnosis. With the use of intraoperative smear preparations and routine stains after paraffin embedding, a correct diagnosis is obtained in more than 90% of cases. Errors result from failure to distinguish between infiltrative gliomas and reactive gliosis, from inappropriate grading of nonhomogeneously composed tumors, and from sampling errors. Future advances in immunohistochemical staining techniques will further facilitate accurate tumor diagnoses by reducing the impact of small sample size obtained by stereotactic technique.

UNUSUAL NEUROMETABOLIC DISEASES OF SAUDI ARABIA, PT Ozand, G Gascon, King Faisal Specialist Hospital and Research Centre, Riyadh

The past experience of the King Faisal Specialist Hospital and Research Centre in regard to the progressive neurodegenerative diseases was presented. Certain unusual diseases are seen frequently in the Kingdom. We have detected ten patients with Sandhoff's disease (GM_2 gangliosidosis, type O) during the past years. A screening test for the disease in Riyadh and in the central region indicates a carrier rate of ten times higher than that seen in the West. We have detected eight families with more than one member afflicted with "ceroid lipofuscinosis" as evidenced by the characteristic inclusion bodies in fibroblasts and the clinical course. We have detected six patients with an unusual form of phenylketonuria (PKU) (biopterin-dependent PKU) among the referred cases. We have found a large number of patients with familial progressive encephalopathy with white matter disease. We have identified: 1, Krabbe's disease; 3, metachromatic leukodystrophies; 1, Zellweger's syndrome; 3, Leigh's disease secondary to the absence of pyruvate carboxylase; and 3, Canavan's disease, but in 18 families no biochemical defect could be established. We have detected other storage diseases that primarily affect the CNS. These are: 1, Hurler's disease; 5, Hunter's disease; 4, San Filippo syndromes; 1, combined sulfatase deficiency (altogether 11 cases of mucopolysaccharidoses with primary CNS involvement); 7, Niemann-Pick disease Type B; 1, Gaucher's disease; and 2 mannosidosis. The large number and the types of storage diseases are substantially different from those reported in the West. These findings should alert pediatricians, primary care physicians, family doctors, and neurologists to these types of neurodegenerative diseases in their practice.

INTERSTITIAL RADIOTHERAPY FOR BRAIN TUMORS, CB Ostertag, Division of Stereotactic Surgery, Department of Neurosurgery, University of Saarland, Homburg, West Germany

The narrow margin between tumor sensitivity and healthy brain sensitivity to radiation considerably limits conventional radiation therapy (teletherapy). Interstitial radiotherapy (brachytherapy) with iodine-125 implants is effective for local tumor control. So far, interstitial radiotherapy using low-activity permanent or temporary implants has been carried out in 225 patients with differentiated gliomas (165 cases) and other tumors (anaplastic gliomas and glioblastomas, 17 cases), ependymomas and papillomas (4 cases), and a variety of other mostly extracerebral tumors (39 cases) in functionally critical cortical or deep-seated locations. Brachytherapy with I^{125} implants is particularly recommended for slowly proliferating, differentiated, nonresectable tumors in functionally critical areas. It enables the surgeon to achieve radiosurgical tumor removal while carefully avoiding radiation and operative damage to healthy brain. Experimental and clinical data make an individualized treatment for each patient desirable.

PATTERN OF STROKE IN THE SAUDI POPULATION AS SEEN AT RIYADH CENTRAL HOSPITAL, NA Pirzada, A Ghafoor, Riyadh Central Hospital

Seven hundred nationals admitted to Riyadh Central Hospital with a diagnosis of stroke were the subject of this study. These patients were analyzed to determine the relative frequency of various types of strokes viz thrombosis, embolism, intracerebral hemorrhage, and subarachnoid hemorrhage. Other variables analyzed were the age and sex distribution, the risk factors for various types of stroke, the vascular territories most commonly involved, the outcome, and prognostic factors influencing outcome. From these data, the important measures for stroke prevention were determined. The data obtained were also compared to those from similar studies conducted in other populations.

THE SO-CALLED "SLOW" VIRUSES, CM Poser, Harvard Medical School, Boston, Massachusetts, USA

Four human diseases due to prolonged viral infection were originally described. More recently, two new ones have been added: AIDS due to HIV and tropical spastic paraparesis due to HTLV-1 infection. The oldest one is what is now known as subacute sclerosing panencephalitis and the organism responsible is a modified measles virus. The disease is disappearing from countries where an obligatory program of vaccination against measles has been introduced. The second one, progressive multifocal leukoencephalopathy, was first described in 1948 but its viral nature was not demonstrated until 1964 by ZuRhein and found to be due to a papovavirus. The third, kuru, was first described in 1957. Because it existed only in the Fore tribe of New Guinea, it was believed to be genetically inherited. A remarkable letter by Hadlow eventually led Gajdusek to achieve transmission of the disease in the laboratory. The virus has not been identified. Kuru seems to be disappearing, possibly because of the interdiction against cannibalism. The fourth one, Creutzfeldt-Jakob disease, has been known for many years as subacute spongiform encephalopathy. The similarity of its neuropathology with kuru led Klatzo to suspect its viral nature. Transmission to man has occurred accidentally on several occasions, but the transmissible agent remains unknown.

THE NEUROLOGICAL COMPLICATIONS OF AIDS AND HTLV-I, CM Poser, Harvard Medical School, Boston, Massachusetts, USA

The neurological complications of AIDS take several forms; the most common one is involvement of the central nervous system by lymphoma or by opportunistic infections such as toxoplasmosis, cryptococcosis, or the papovavirus of progressive multifocal encephalopathy. A second neurological complication is a true encephalitis, with the formation of pathognomonic multinucleated giant cells which actually contain HIV. An encephalopathy which is neuropathologically identical with postinfectious perivascular demyelinating leukoencephalopathy is almost always present along with the HIV invasion but is secondary to the immune response provoked by the virus. It is because of this type of lesion that treatment with corticosteroids has been suggested. In addition, myelopathies and peripheral neuropathies may also occur either in conjunction or independently. The peripheral neuropathies have been reported as responding to treatment with corticosteroids. HTLV-1 causes tropical spastic paraparesis, which is known in Japan as HTLV-associated myelopathy. Although the main manifestation is a slowly progressive paraparesis, other parts of the nervous system are often involved. The disease is endemic in various parts of the world and is difficult to differentiate from multiple sclerosis. However, the single report that HTLV-1 may actually cause multiple sclerosis has been completely disproved by a number of quite reliable investigators.

THE BIRTH OF STEREOTAXIC SURGERY AT THE KING FAISAL SPECIALIST HOSPITAL AND RESEARCH CENTRE, B Rahm, IN Kanaan, J Brismar, A Haider, A Jallu, E Siqueira, Department of Neurosciences, King Faisal Specialist Hospital and Research Centre, Riyadh

With the evolution of the new neuroradiological techniques (computed tomography [CT] and magnetic resonance imaging [MRI]), stereotaxic surgery became a well-established practice in modern neurosurgery, drawing the guidelines for its use as an effective treatment such as radiation, medical antituberculosis, antifungal, and extensive surgery. We report here our experience with CT-guided stereotaxic biopsy in a series of patients with brain mass lesions (aged 5 to 68 years old), referred to King Faisal Specialist Hospital and Research Centre. The indication for the procedure was restricted to deep-seated lesions (brainstem, thalamus), lesions in eloquent areas of the brain, patients with poor general medical condition, and patients whose radiological studies were not conclusive enough to start an effective treatment. All procedures were performed with patients under general anesthesia. The set-up was such that the biopsy operation could be converted to a "regular" craniotomy if necessary. The coordinates of the targets (x, y, z) were measured by CT scan and rechecked by the surgeon on the computer in the operating room. To monitor the area of the biopsy, we used the intraoperative x-ray and early CT follow-up. In our series, the mortality and surgical morbidity were nil. The technique will be improved in the future, with plans to implement MRI-guided stereotaxic surgery. Functional neurosurgical procedures are also feasible with the CT- and MRI-guided stereotaxic surgery.

REHABILITATION OUTCOME OF SPINAL CORD INJURED (SCI) PATIENTS TREATED IN THE REHABILITATION UNIT, ARMED FORCES HOSPITAL, RIYADH, SAUDI ARABIA, CAT Rajan, Riyadh Armed Forces Hospital

The case histories of 250 spinal cord injured (SCI) patients treated in this unit between November 1982 and September 1988 were reviewed. The age, sex, marital status, pre-injury social and vocational status, cause of SCI, level of neurological status, degree of completeness, duration of paralysis on admission to the rehabilitation unit, and associated injuries were compared with the functional outcome and social re-integration after comprehensive rehabilitation training. The management of the SCI patients in general hospitals prior to arrival at the rehabilitation unit and complications acquired from the general hospitals were briefly studied. The disadvantages of managing SCI patients in a general rehabilitation unit compared with a specialized spinal unit were analyzed.

TRAUMATIC INTRACRANIAL EXTRADURAL HEMATOMA: ASSOCIATED CT SCAN ABNORMALITIES INFLUENCING PROGNOSIS: EXPERIENCE IN RIYADH CENTRAL HOSPITAL, DRK Reddy, Riyadh Central Hospital

Acute extradural hematoma is the only entity from which a patient can fully recover afer surgery, even after gross deterioration, but we found a number of associated lesions that reduced the rate and quality of recovery and even led to death. The advent of CT scanning has unearthed a number of these associated lesions. We observed a number of them during the last six years at Riyadh Central Hospital. A CT scan is invaluable in making the assessment.

ANALYSIS OF 30 CASES OF ACUTE UNILATERAL MYDRIASIS (WITHOUT INDICATION FOR SURGERY) SEEN IN NEUROSURGICAL EMERGENCY ROOM, R.C.H., DURING 1408H, DRK Reddy, Riyadh Central Hospital

It is a great puzzle for a neurosurgeon when he or she encounters a case of unilateral papillary dilatation as an acute emergency, especially if there is no CT scan to assist in the evaluation. The majority of our nonneurological colleagues have a fixed idea that these must be extradural hematomas. This study is to convince them that a variety of other lesions on even normal scans may be associated with unilateral papillary dilatation. All unilateral papillary dilatations may not represent surgically treatable lesions. At the same time, inadvertent "woodpecker" surgery may be totally useless and more damaging. A total of 30 cases of traumatic unilateral mydriasis seen during one year were studied and none needed operation. Each case was discussed, enlisting the radiological findings and stressing the need for a CT scanner at every center.

HEADACHE SYNDROMES IN THE EASTERN PROVINCE OF SAUDI ARABIA: A STUDY OF 224 SUBJECTS, S Al-Rajeh, O Bademosi, A Awada, H Ismail, M Adham, Department of Neurology, King Faisal University, Dammam

Headache is a common global problem which causes a lot of distress to the sufferer. This report describes our study to delineate the various clinical variants and etiologic factors in subjects in whom headache was the primary or main feature and evaluated by the Neurology Department, KFHU, Khobar, as part of a prospective study. During the study period, 224 subjects (142 Saudi nationals: 64 males, 75 females, aged 15-72 years; 82 non-Saudis: 50 males, 32 females, aged 12-57 years) with headache syndromes accounted for 13% of all neurological cases. Headache syndromes were rare in those under the age of 10 years (0%) and above 50 years old (4%). Tension headache (65%) was the most common clinical type. Migraine, encountered in 62 subjects (28%), was more frequent in males (58%) than females (42%) for all age groups, except in the fourth decade in Saudi nationals. Benign raised intracranial pressure, though uncommon, showed a female predilection. Other unusual causes included sinusitis, temporomandibular joint, ocular disorders, and tumors. The clinical features and social implications of our findings were discussed.

ANALYSIS OF EXPERIENCE WITH 236 SHUNT OPERATIONS FOR HYDROCEPHALUS IN RIYADH CENTRAL HOSPITAL OVER A PERIOD OF 3 YEARS 1406-1408H, DRK Reddy, Department of Neurosurgery, Riyadh Central Hospital

The incidence of hydrocephalus is very high in the Kingdom of Saudi Arabia. It is the most common pediatric neurosurgical operation performed in Riyadh Central Hospital: 236 shunt operations were done for hydrocephalus over a period of 3 years (1406-1408H), including both congenital and acquired hydrocephalus. We have had no operative or immediate postoperative deaths. The immediate operative and postoperative complication was bleeding along the valve tube due to preexisting bleeding disorder in not more than 2 cases (less than 1%), predominantly affecting Saudis. Our technique will be described. The nature of lesions producing acquired hydrocephalus was outlined for 119 cases. There was also discussion about our preference in selecting the shunt pressures and placement.

LUMBAR CANAL STENOSIS AND/OR NERVE ROOT CANAL STENOSIS IN RELATION TO BACK PROBLEMS, AM Sabbagh, Neurosurgery Department, Riyadh Central Hospital

A personal series of 134 cases of spinal cord surgery performed at Riyadh Central Hospital over about two years is reviewed. Different surgical approaches are discussed in relation to the existing pathology. In all cases, the surgery was performed with the aid of a surgical microscope. Simple disc prolapses were dealt with by interlaminar fenestration. Extensive decompressive laminectomies and bilateral foraminectomies were performed for all cases of spinal canal and nerve root canal stenosis. Isolated nerve root canal stenosis was treated surgically with extensive bilateral foraminectomies. In some cases of spinal canal and/or nerve root canal stenosis, disc evacuation was also performed according to the intraoperative finding. Overall assessment of the different pathologies and surgical procedures was reviewed and results were analyzed. Twenty-nine percent of all patients had stenotic elements of the spine producing disabilities during the productive period of life. Of these, 2/3 were stenotic lesions of the spinal canal and 1/3 were of the root canals. The majority of the patients with spinal canal stenosis were males between 30 and 40 years of age, whereas the majority of patients with nerve root canal stenosis were males between 40 to 50 years. Decompressive procedures performed at our facility have considerably helped these patients, so that about 90% of them have returned to normal life.

JUVENILE MYOCLONIC EPILEPSY: A STUDY OF THE FACTORS RESPONSIBLE FOR THE MISDIAGNOSIS IN AN EPILEPTIC CLINIC, AR Al-Tahan, CP Panayiotopoulos, T Obeid, Division of Neurology, King Khalid University Hospital, Riyadh

Juvenile myoclonic epilepsy is a well-defined epileptic disease with characteristic clinical and EEG findings. Despite this, it is misdiagnosed worldwide, with considerable consequences regarding management, in particular, drug choice and prognosis. This study identified the factors behind misdiagnosis. Seventy cases were analyzed, of which 66 (91.4%) were misdiagnosed and on referral 22 (31.4%) were missed by epilepsy clinic. To reach a correct diagnosis, it took 17.7 ± 10.4 months for the epilepsy clinic on the first evaluation and 8.3 ± 5.5 years from first reported fit. The following factors contributed to the delay in diagnosis: myoclonic jerks not revealed by appropriate questioning, 14; myclonic jerks revealed but not appreciated, 2; myoclonic jerks not revealed despite proper questioning, 2; unilateral jerks, 4; EEG "typical" though not appreciated, 11; EEG typical but with focal abnormalities, 3; EEG with nonspecific abnormalities or normal, 8. We believe that direct questioning may frequently reveal the presence of mild myoclonic jerks that are considered irrelevant by the patient. A suspicious clinical setting should prompt such questioning even if the EEG was normal, but especially when it shows typical changes. Awareness of the possibility of unilateral jerks or focal EEG changes will guard against misdiagnosing the disorder as simple or complex partial seizures.

MULTIPLE SCLEROSIS IN SAUDI ARABIA, B Yaqub, S Al-Deeb, AK Daif, M Jaberi, AR Al-Tahan, H Sharif, Neurology Units at King Khalid University Hospital and Riyadh Armed Forces Hospital

There are indications of increasing incidences of multiple sclerosis (MS) in Saudi Arabia. In the last 5 years, we have evaluated 33 native-born (KKUH) Saudis with definite MS at King Khalid University Hospital and Riyadh Armed Forces Hospital (RAFH). In one hospital (KKUH), they constitute 2% of all inpatient admissions, with a prevalence of eight per

100,000 population (hospital series). There is a strong female preponderance, with a female/male ratio of 4:1. The presenting clinical features were numbness and paresthesia, 50%; diplopia, 60%; paraplegia, 20%; hemiplegia, 10%; monoparesis, 10%; optic neuritis, 22%; gait disturbances, 19%; and bladder disturbances, 2%. The sites of lesion as evidenced clinically or paraclinically were spinal (70%), brainstem (60%), optic (65%), cerebellar (40%), and cerebral (40%). PSVEPs were abnormal in 65% and BAEPs were abnormal in 45% of the patients. Brain CT scan showed single or multiple white matter, low-attenuation areas in 10% and generalized brain atrophy in 5%, with overall abnormality in 15%. MRI was done in 15 patients and all scans were abnormal. CSF showed pleocytosis in 40% and raised protein in 25%. IgG index was done in 20 patients and was abnormal in 15. CSF IgG oligoclonal bands were found in all 15 patients who had the test. Though the symptomatology and site of lesions are similar to those in the West, the course and evolution were different. The main course was remissions and relapses with very few transformed to the chronic progressive form, and the main disability was partial or complete bilateral visual loss, seen in 20% of the patients.

THE RECENT ADVANCES IN THE MANAGEMENT OF BONE TUMORS

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HISTORICAL NAMES IN BONE TUMORS, MI Dhebar, King Khalid University Hospital, Riyadh

"If I have seen further... it is by standing on the shoulder of giants." [Sir Isaac Newton, 1675]. The use of proper names are common in medicine. Syndromes, signs, and tests are given the names of their discoverers or elaborators, and operative procedures, incisions, and even a system of treatments come to be known by proper names. Surgery for bone tumors is a field of special interest, a combination of plastic and orthopedic surgery. For instance, there is Codman's triangle and Bence Jones Protein. But there are other aspects to the use of a person's name, and that is, how and in what circumstances did they accomplish the work, what did they do to justify such recognition, and who or what provided the stimulus. Pliny the Elder (Roman scholar, AD 23-79) said that no man possesses such genius that he can become commanding unless a subject suited to his talents presents itself and an opportunity occurs for its development. Time has a way of putting things into perspective and some names used so freely today will disappear, whereas less well known names may later be recognized for some valuable contribution. Attempt has been made to trace the notable names and their contribution in the treatment of bone tumors.

THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE MANAGEMENT OF BONE TUMORS, HS Sharif, Department of Radiology, Riyadh Armed Forces Hospital

Magnetic resonance imaging (MRI) has recently been shown to be extremely useful in the management of musculoskeletal neoplasms. The high-contrast resolution, direct multiplanar capability, and lack of ionizing radiation make MRI effective in evaluating these diseases. In the arm, leg, and foot MRI can define the extent of the soft tissue mass to better advantage than computed tomographic (CT) scanning. Intramedullary extension is also better defined by MRI than CT or bone scintigraphy. MRI can easily differentiate hyperemic osteoporosis from intramedullary tumor spread, which is not possible with other available imaging modalities. MRI is more useful than CT and at least as good as angiography for assessing vascular and joint involvement. Certain tumors of cartilage, fat, angiomatous, and fibrous origins have characteristic features of MRI. Therapy planning and post-therapy follow-up can ideally be performed by means of MRI since MRI has the unique ability to monitor changes within the tumor mass that are secondary to treatment. Early recurrence can also be easily depicted. MRI is currently the most sensitive modality for staging of primary bone tumors. Post-therapy assessment is also easily achieved in a way that is advantageous to conventional techniques.

PROSTHETIC REPLACEMENT IN BONE TUMOR SURGERY, R Capanna, G Bettelli, M Manfrini, A Ferraro, R De Cristofaro, M Campanacci, The Bone Tumor Center, Istituto Ortopedico Rizzoli, Bologna, Italy

Since 1974 at the Instituto Ortopedico Rizzoli, reconstruction after resection of the proximal humerus for bone tumor is done using modular rotatory endoprostheses. Up until 1986, 94 prostheses had been implanted. There were 64 primary malignant bone tumors, 11 aggressive benign tumors, and 19 bone metastases. In 60 cases an intra-articular and in 34 a classic or modified (trans-scapular) Tikhoff-Linberg extra-articular resection was performed. The prosthesis was anchored to the acromion or, in Tikhoff-Linberg procedures, to the clavicle stump. In five cases deep infection developed and necessitated removal of the prosthesis. In three cases the cortex was perforated while reaming the medullary canal, with consequent extrusion of the cement. The patients were able to do sedentary work, always with their hand below the shoulder level, due to impairment of active abduction. Active rotations were normal. At a follow-up of one to 14 years (average, four), there was no loosening of the prosthetic stem in any of the patients. Kotz modular cementless prostheses have been implanted since 1983 at the Istituto Ortopedico Rizzoli after lower limb resections for bone tumors. Up until 1987, 100 patients were operated on. The prostheses replaced the proximal femur in 26 cases, the distal femur in 66, the proximal tibia in seven, and the entire knee joint in one. The lesions were: 15 benign tumors, 83 malignant tumors, one Charcot joint, and one bone metastasis. At the proximal femur, in two cases the resection was extra-articular and reconstruction of the acetabulum was performed with bone grafts. In proximal tibia resections, the patellar tendon was anchored to the prosthesis and sutured to the anteposed gastrocnemius. The most important complications were five deep infections, four SPE palsies, one hip dislocation, one loosening of the acetabular component, and one fracture of the prosthetic stem; both latter complications required revision of the implant. Analysis of the radiographic evolution of the stem fixation led to modifications of the implant fixation component.

PELVIC RESECTIONS, R Capanna, G Bettelli, M Manfrini, A Ferruzzi, R Casadei, M Campanacci, The Bone Tumor Center, Instituto Ortopedico Rizzoli, Bologna, Italy

From 1968 to 1986, 77 pelvic resections were performed at the Instituto Ortopedico Rizzoli for primary bone lesions. There were 35 low-grade and 38 high-grade sarcomas, three benign but aggressive tumors, and one hydatid cyst. Pelvic resections were divided according to Enneking's classification: type A (iliac wing resections, 27 cases), type B (periacetabular resections, 36 cases), and type C (anterior arch resections, 14 cases). Subdivisions of each type in classes were operated on according to the extension of the resection and the kind of reconstruction. At a mean follow-up of seven years (range, two to 14 years), the oncological results were satisfying for benign and low-grade tumors (100% and 86% disease-free patients, respectively). For high-grade tumors and Ewing's sarcoma the rates for disease-free patients were 42% and 21%, respectively. Complications were frequent after pelvic resections. The infection rate was 25%. Vascular damages were more frequent after periacetabular resection, including the anterior arch; urogenital complications were seen with anterior arch resection, and neurological damages were associated with iliac wing resection. Functional results were strictly dependent on the type of resection; they were usually excellent in type C and type A resections, provided the pelvic ring had not been interrupted. Results were usually fair in type B resections and in type A resections after interruption of the pelvic ring or neurological damage. The complexity of most pelvic resections and the amount of complications suggest the procedure should be restricted to low-grade malignant tumors, especially chondrosarcomas.

THE PLACE OF COMPUTED TOMOGRAPHY IN THE MANAGEMENT OF BONE TUMORS, J Pooley, Department of Orthopedic Surgery, University of Newcastle upon Tyne, United Kingdom

Improvement in imaging techniques has been an important factor in the evolution of limb preserving procedures for bone tumors, as the ability to define the precise site and local extent of a tumor is necessary for planning the definitve surgical procedure. Debate about the best technique is unproductive, because each has its own advantages and disadvantages. For example, the images obtained by computed tomography (CT) are inferior to plain radiographs for identifying the precise site and nature of a tumor involving a long bone. However, in some areas of the skeleton (e.g. spine and pelvis) in which superimposition of the bones is seen on plain radiographs, CT may demonstrate a lesion that is not visible on these. The important feature of CT in the staging of bone tumors is its ability to demonstrate the extent of the local disease, both within the marrow cavity and out into the soft tissues. Enhancement with contrast medium demonstrates the relationship of extraosseous tumor to major neurovascular structures, enabling the feasibility of a limb preserving procedure to be assessed. In the presence of a metal prosthesis, the CT image is often completely obscured by artifact. This limitation does not apply to magnetic resonance imaging (MRI), which in other respects has been found to be superior to CT in evaluating the local extent of musculoskeletal tumors. However, the ability of CT to detect lung metastases too small to be seen on plain radiographs is now well established. CT is superior to MRI in detecting pulmonary metastases, as these lesions are obscured by normal lung movements during the relatively long period required to collect data necessary to perform an MRI study. CT scanning was carried out during staging of 25 cases of aggressive or malignant bone tumors resected in the Department of Orthopaedic Surgery, Newcastle upon Tyne, UK, and detailed examination of the resected specimens compared with the CT images. In one case the CT scan was interpreted as demonstrating intra-articular extension of tumor where none was found at operation. The level of intramedullary extension of tumor determined by CT scan corresponded well with the extent of tumor demonstrated histologically, which allowed safe resection margins to be determined preoperatively. Although MRI is now superseding CT in evaluating the local extent of musculoskeletal tumors, CT examination of the lungs remains essential in the initial staging of bone tumors and during the follow-up of patients after treatment.

SURGICAL STAGING MUSCULOSKELETAL NEOPLASMS (ENNEKING), RJ Rooney, Department of Orthopedic Surgery, King Faisal Specialist Hospital and Research Centre, Riyadh

In the September 1980 issue of the *Journal of Bone & Joint Surgery*, Enneking et al published the surgical staging system of musculoskeletal sarcoma. His group believed there was a need for standard and commonly accepted terminology defining surgical stages, surgical procedures, and management of data. The purpose of this staging system was to compare lesions with a similar prognosis and to evaluate the methods of management. We present the Enneking Surgical Staging System of musculoskeletal neoplasms that has been utilized at the King Faisal Specialist Hospital and Research Centre since 1983.

ORTHOPEDIC TUMORS: King Faisal Specialist Hospital and Research Centre, RJ Rooney, Department of Orthopedic Surgery, King Faisal Specialist Hospital and Research Centre, Riyadh

This presentation addressed the evaluation and treatment of musculoskeletal tumor cases referred to the King Faisal Specialist Hospital and Research Centre, a tertiary care center, from 1975 to the present. An overview of the orthopedic oncologic management here in Saudi Arabia was presented.

GIANT CELL TUMOR, R Capanna, G Bettelli, M Manfrini, N Fabbri, R De Cristofaro, M Campanacci, The Bone Tumor Center, Instituto Ortopedico Rizzoli, Bologna, Italy

From 1913 to 1983 at the Instituto Ortopedico Rizzoli, 293 patients were treated for giant cell tumor of bone. In about two thirds of the cases the distal femur or proximal tibia were involved. Patient age ranged from 20 to 50 years in 78% of the cases, and no sex preponderance was evident. The tumor commonly involved the metaphysis and the epiphysis, was occasionally limited to the metaphysis, and in 2% of cases grew adjacent to an open growth plate on the metaphyseal side. In 5% of cases the adjacent bone was invaded through the joint space by the tumor. A radiographic grading was used, classifying the tumors into three groups: grade 1 (latent) in 4%, grade 2 (active) in 74%, and grade 3 (aggressive) in 22% of cases. The rate of recurrence after surgical treatment was 27% after intralesional procedures (curettage), 8% after marginal procedures, and nil after wide or radical procedures. These results did not correlate with the radiographic grade of the lesion. Surgical adjuvants (cement, phenol, cryosurgery) were used in 8% of cases. This technique (curettage, phenol, and cement) has recently become the recommended one for grade 1 and grade 2 lesions. Six patients had pulmonary metastases and in one the outcome was unfavorable. In ten patients a sarcoma developed at the site of a previously documented benign giant cell tumor. Eight received radiation therapy exceeding 40 Gy.

LIMB PRESERVING PROCEDURES USING THE KOTZ MODULAR PROSTHESIS: THE NEWCASTLE EXPERIENCE, J Pooley, Department of Orthopaedic Surgery, University of Newcastle upon Tyne, United Kingdom

Between September 1984 and April 1988, 16 patients with primary malignant tumors involving either femur or tibia underwent resection of their tumor and reconstruction using the Kotz Modular Prosthesis (Howmedica UK Ltd.). One further patient, who had undergone previous limb preserving surgery with another type of prosthesis which had required revision, underwent a further revision to a Kotz prosthesis three years after the original surgical procedure. All the operative procedures reported in this series were carried out in the University Department of Orthopaedic Surgery, Newcastle upon Tyne. There were nine male and seven female patients, with a mean age of 20 years (range, 12-62 years). The histological diagnosis was osteosarcoma in nine patients, chondrosarcoma in five, and Ewing's sarcoma, giant cell tumor, and malignant schwannoma in one patient each. The segment of bone resected was the distal femur in 11 patients, proximal femur in two, total femur in three, and proximal tibia in one patient. Preoperative chemotherapy had been administered in seven patients and preoperative radiotherapy in one. Histological examination of the resected specimens demonstrated that wide margins had been achieved in 15 patients and a marginal excision in one. Eleven patients were alive at the time of review, with a mean follow-up of 27.5 months (range, 6-49 months). The review was performed by an independent observer who had not been involved in treatment. Major complications included deep infection in four patients. Three patients underwent subsequent amputation. There was mechanical failure of the prosthesis in one patient that was successfully revised. Of the 11 surviving patients, one had undergone amputation and one had become paraplegic due to spinal metastases. The remaining nine patients were assessed and graded according to the system of Enneking. Two patients were graded as excellent, four as good, and three as poor. All patients interviewed stated that they would opt for a limb preserving procedure again.

GENERAL CONSIDERATIONS OF LIMB PRESERVING SURGERY IN THE TREATMENT OF BONE TUMORS, J Pooley, Department of Orthopaedic Surgery, University of Newcastle upon Tyne, United Kingdom

Continuing improvements in chemotherapy for some malignant bone tumors have led to an increased probability of cure. There is, therefore, an increasing interest in limb preserving (sparing/salvage) types of procedure in order to preserve function. Nevertheless, some surgeons remain unconvinced that any surgical procedure other than amputation can be safely recommended in the treatment of a malignant bone tumor. The controversy over amputation versus conservative surgery can be resolved if we approach treatment by first clearly defining the aims of surgery and then considering the behavior of the tumor within the tissues. In this way we may select an operative procedure that will meet the aims. A fundamental concept expressed by Enneking is that the behavior of the various musculoskeletal tumors passes through a series of stages from benign to metastatic malignant disease. The stage a tumor has reached is arrived at by considering its surgical grade, site, and local extent, and the presence or absence of metastases. The stage of a tumor is determined by appropriate imaging studies followed by biopsy. The principal aim of surgery is to completely excise the primary lesion; secondary aims are to preserve the maximum function and appearance of a limb. Irrespective of the type of bone tumor, successful treatment depends on a surgeon performing an adequate surgical procedure. The question therefore arises "what constitutes an adequate surgical procedure?" Enneking has graded surgical procedures on a scale of 1 to 4, which correlates with his staging system. A Grade 3 surgical procedure describes a wide excision and Grade 4 denotes radical margins. It is possible to achieve the same surgical margins through either amputation or resection. It has also been shown that, in patients with malignant bone tumors, the prognosis following wide excision is equivalent to that following radical surgery. Grade 3 is the minimal surgical treatment for a malignant bone tumor. If after appropriate staging studies, it is considered that this can be achieved and yet preserve sufficient muscle function and the neurovascular status of the limb, then a limb preserving procedure is a logical treatment. The most appropriate limb preserving procedure, rotationplasty, resection arthrodesis, allograft transplantation, or endoprosthetic replacement, is chosen by assessing the needs of each patient.

BIOPSY TECHNIQUE, J Pooley, Department of Orthopaedic Surgery, University of Newcastle upon Tyne, United Kingdom

The firm diagnosis of a musculoskeletal tumor depends on its recognition through microscopic examination of material obtained by biopsy. Definitive treatment of a presumed malignant tumor should therefore never be carried out until the diagnosis has been confirmed by a pathologist experienced in the recognition of these tumors. A poor technique for obtaining biopsy material may have a profound effect on subsequent surgical treatment. For example, obtaining unrepresentative material may lead to error in diagnosis. Furthermore, a poorly placed biopsy incision may prevent a limb preserving procedure or even a radical amputation being carried out. As the biopsy incision must integrate with the planned definitive surgical procedure, the biopsy should be carried out by the surgeon who intends to perform the surgery. When considering the timing of biopsy in relation to the other staging studies, it must be remembered that the accuracy of imaging techniques in demonstrating the local extent of a tumor is impaired by distortion of the tissues as a result of surgical biopsy. Biopsies should therefore be performed after the other staging studies have been completed. Because of the risk of disseminating malignant cells by performing a biopsy, the interval between this and the definitive procedure should be kept as short as possible. The site of the biopsy incision must allow the preferred surgical option to be carried out; therefore: (1) always use a longitudinally placed incision in a limb; (2) avoid approaching major neurovascular structures; and (3) the biopsy track should run through a muscle belly rather than in the plane between muscles. Biopsy material may be obtained by either closed needle biopsy or open incisional biopsy. Closed biopsy allows only a small amount of tissue to be obtained, and this may lead to errors in diagnosis or staging of those tumors which are not homogeneous. Closed biopsy is therefore better for lesions in less accessible surgical sites. Open biopsy allows an amount of tissue to be obtained sufficient to minimize sampling error. This is therefore the preferred technique for primary tumors involving limbs. When carrying out an open biopsy, (1) use the smallest incision consistent with obtaining adequate amounts of tissue; (2) sample material from the periphery of the tumor, remembering that the central regions are often necrotic; and (3) include material from the interface of the lesion and its capsule or pseudocapsule. Meticulous hemostasis prevents the local spread of malignant cells within a postoperative hematoma. Avoid the use of the wound drain as the drain site would have to be included en bloc in subsequent resection. Biopsy is the essential final step in staging a musculoskeletal tumor. Errors in technique may compromise the definitive surgical procedure, leading to amputation when perhaps a limb preserving operation could have been performed.

MODERN MANAGEMENT OF OSTEOSARCOMA, AW Craft, Departments of Paediatrics and Oncology, University of Newcastle upon Tyne, United Kingdom

Osteosarcoma has been reported in a child of three years and can occur at almost any time during adult life, but the peak age of incidence is between 10 and 20 years. Many tumors occurring in later life complicate Paget's disease, which does not occur in children. The annual incidence of the tumor in children is reported at about two per million children under 15 years and is more common in males than females (1.6 to 1). Diagnosis of osteosarcoma is made by biopsy and a plan of management can then be formulated for the particular patient. This will depend on the age of the patient, the site of the tumor, and the presence or absence of metastases. There should be a full pre-treatment evaluation including computed tomographic scan of the lungs. Prior to the advent of chemotherapy, only about 20% of osteosarcoma patients could be cured, usually by amputation. During the past 20 years there have been numerous reports of improved survival rates obtained with various chemotherapy combinations. There were also reports at one stage of improved survival rates with surgery alone. However, two randomized studies have now shown the clear benefit for chemotherapy. The three most active drugs in the management of osteosarcoma are methotrexate, cisplatin, and Adriamycin and most modern regimens will include at least two of these drugs, sometimes with the addition of bleomycin, cyclophosphamide, and actinomycin. Rosen has reported the best survival figures using the T10 protocol. The philosophy behind this regimen is that initial chemotherapy is given with high-dose methotrexate and the tumor is removed following this therapy. A pathological grading is carried out according to the degree of necrosis of the tumor, and subsequent chemotherapy is based on the preoperative pathological response. Those who have a good response continue a methotrexate-based regimen, whereas those who have a poor response switch to an Adriamycin/platinum-based regimen. In multi-institutional studies conducted in the United States, survival rates of around 70% have been achieved at three years. The European Osteosarcoma Intergroup has been attempting to find simpler and shorter methods of treatment and the EOI-1 Study compared cisplatin and Adriamycin with or without high-dose methotrexate. The survival rates for the two drug arms were as good as those achieved in the United States using a Rosen type of protocol, and the current EOI study is now comparing the two-drug combination of cisplatin/Adriamycin against a Rosen type of regimen in a randomized study. Ifosfamide is the main new agent which is being considered for the management of osteosarcoma.

CURRENT MANAGEMENT OF EWING'S SARCOMA, AW Craft, Departments of Paediatrics and Oncology, University of Newcastle upon Tyne, United Kingdom

Ewing's sarcoma is rare, with an annual incidence estimated at 0.6 per million population. It occurs throughout the world but is extremely uncommon in Negro races. The management of Ewing's sarcoma depended for many years on either surgical amputation or radiotherapy. Long-term survival using this approach was poor, with a 15% or less cure rate. Significant improvements in survival did not occur until the advent of chemotherapy. Survival rates of up to 60% have been achieved in large multi-institutional studies, although even better survival rates are reported from single institutions. The prognosis for Ewing's sarcoma is dependent on several prognostic factors. The most important of these is the presence or lack of metastases at the time of diagnosis. Second, the site and size of the tumor are important in tumors of the axial skeleton, with those affecting the pelvic bones having the worst prognosis. Larger tumors have a worse prognosis than smaller ones, and the pelvic site and large tumors tend to go together. Older patients tend to have a worse prognosis, but there is no difference in the outcome according to sex. An elevated serum lactic dehydrogenase activity at diagnosis has been reported as a poor prognostic factor, but has not been substantiated by others. Treatment consists of combination chemotherapy and radiotherapy and there is a growing trend toward surgical removal of tumors whenever possible. The most active chemotherapy agents are vincristine, Adriamycin, actinomycin D, cyclophosphamide, ifosfamide, and VP16, and most current therapeutic regimens include drugs taken from this group. In the United Kingdom, the treatment is based largely on ifosfamide, with the addition of vincristine, Adriamycin, and actinomycin D. Surgery is considered for all cases, and if complete surgical resection has been achieved, then radiotherapy may be omitted. The dose of irradiation is tailored to the site and size of the original tumor. The late effects of treatment (e.g., pathological fracture) through irradiated bone and limb shortening must be considered in the design of protocols of treatment for Ewing's sarcoma.

THE ORGANIZATION OF A BONE TUMOR SERVICE, AW Craft, Department of Paediatrics and Oncology, University of Newcastle upon Tyne, United Kingdom

The management of bone tumors is a prime example of a multidisciplinary approach. A prerequisite for the organization and evaluation of a service is the accurate registration of all cases occurring within a defined population. This requires the setting up of a bone tumor registry, primarily organized by a pathologist. This registry can act as a focal point for the organization of a bone tumor service. Regular meetings can be organized with all of the disciplines involved, and this can serve both a management and education function. Specialists involved should be: pathologist, orthopedic surgeon, radiologist, oncologist/radiotherapist, and rehabilitation staff. Bone tumors are rare and the expertise to manage them needs to be centralized. The size of region necessary to generate sufficient work to build up excellence in bone tumor management depends on many factors, including distance from the nearest center. However, a population of 5 million people should generate sufficient work to enable establishment of a comprehensive bone tumor service.

FROM "CURE AT ANY COST" TO "CURE AT LEAST COST": THE LATE EFFECTS OF TREATMENT, AW Craft, Departments of Paediatrics and Oncology, University of Newcastle upon Tyne, United Kingdom

Twenty years ago few patients with a bone tumor survived, so that the late effects of treatment was of little consequence. However, now that well over half of all bone tumors in young people can be cured, it becomes increasingly important to look at the consequences of the cure. The physical problems associated with the tumor itself may result from mutilating surgery, (e.g., amputation) or the late effects of radiotherapy. Radiotherapy is widely used for the management of Ewing's sarcoma, and the resultant growth defects can be considerable. In addition, radiotherapy can cause late necrosis of the bone, which if it is already diseased can result in pathological fracture. Chemotherapy is increasingly used in the management of both osteosarcoma and Ewing's sarcoma, and we are only just beginning to recognize the late consequences of such therapy. These may be organ specific (e.g., renal damage due to cisplatin) or infertility due to cyclophosphamide, or they may be more general. Second primary tumors are an additional late consequence of the management of bone tumors. These may occur in individuals who have a genetic predisposition to cancer or be a consequence of the treatment itself. Prolonged follow-up of survivors of cancer in early life is essential so that the late consequences of the treatment can be recognized and treatment modified for subsequent generations.

Announcements

The *Annals of Saudi Medicine* is pleased to publish announcements of educational opportunities of interest to its readers. For adequate publicity, notices of postgraduate courses, meetings, and lectures must be received at least 6 months before the date of occurrence. Please send relevant information to the *Annals of Saudi Medicine*, Publications Office, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia.

King Saud University Fellowship in Pathology

King Saud University announces the inception of a 5-year joint fellowship training program in pathology. The training will be at King Khalid University Hospital, King Faisal Specialist Hospital and Research Centre, and Riyadh Armed Forces Hospital, and is a full-time program. Application is open to interested and suitably qualified residents from all over the Kingdom. To be eligible, applicants will meet the following criteria:

1. Doctors who hold MB,BS from King Saud University or equivalent degree with at least Good grade.
2. Doctors who have finished their internship in a recognized hospital with at least a Very Good grade.
3. Successful completion of a selection examination and personal interview.
4. Applicants from other institutions should submit a letter from his/her employer that he/she will be sponsored during the whole period of training.

Applications and inquiries should be sent to the Director, Postgraduate Medical Education, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia.

King Faisal Specialist Hospital and Research Centre Postgraduate Training Programs

King Faisal Specialist Hospital and Research Centre is pleased to invite applications for the following full-time postgraduate training programs:

1. Arab Board residency training in the specialties of internal medicine, obstetrics/gynecology, pediatrics, and surgery.
2. Five-year pathology residency training program, affiliated with the Royal College of Pathologists of Australasia and the King Saud University.
3. Fellowships, both adult and pediatric, in cardiology, endocrinology, gastroenterology, infectious diseases, nephrology, hematology, and oncology. Also, adult pulmonary and critical care medicine, adult rheumatology, pediatric allergy and clinical immunology, neonatal/perinatal medicine, and pediatric neurology.

For further information contact the Director, Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia; telephone (01) 464-7272, extension 1837.

Radiopharmaceuticals from King Faisal Specialist Hospital and Research Centre

King Faisal Specialist Hospital and Research Centre manufactures various radiopharmaceuticals at its Radionuclide and Cyclotron Operations facility with the aid of model CS-30 Cyclotron. These radiopharmaceuticals are produced according to international standards of good manufacturing practice. The Research Centre meets the high standards of quality assurance and environmental safety with regard to radiopharmaceuticals.

Radiopharmaceuticals currently produced and available for distribution throughout the Kingdom and to adjoining Arab states are as follows: thallous (Tl-201) chloride injection ($T^{1/2}$ = 73 h); gallium (Ga-67) citrate injection ($T^{1/2}$ = 78.3 h); iodine-123 capsules ($T^{1/2}$ = 13.1 h); iodine-123 oral solution ($T^{1/2}$ = 13.1 h); iodine-123 orthoiodohippurate solution ($T^{1/2}$ = 13.1 h); rubidium (Rb-81) → krypton (Kr-81 m) generator ($T^{1/2}$ = 4.58 h – 13 s); indium (In-111) oxine ($T^{1/2}$ = 67.92 h) for cell labeling; indium (In-111) DTPA for cisternography ($T^{1/2}$ = 67.92 h).

Suggestions from the medical community for additional cyclotron-produced needs are welcome.

Inquiries concerning the availability, price schedule, and technical information on specific radiopharmaceuticals should be directed to: Abbass H. Al-Marzouky, MD, Executive Director, Research Centre, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia (Fax No. 966-1-441-4839).

Joint Board for Postgraduate Medical Education Symposia

The Joint Board for Postgraduate Education is pleased to announce the following symposia for 1410-1411 (1989-1990):

1. Recent Advances in Infectious Diseases, King Fahad National Guard Hospital, Riyadh, 25-26 Shawwal 1410 (20-21 May 1990).
2. Advances in Obstetrics & Gynaecology, Riyadh Armed Forces Hospital, 4-5 Rabi Al-Awal 1411 (23-24 September 1990).
3. Advances in Diagnostic Radiology, King Faisal Specialist Hospital and Research Centre, 11-12 Rabi Al-Awal 1411 (30 September-1 October 1990).
4. Advances in Thrombosis, King Faisal Specialist Hospital and Research Centre, 15-16 Jumada Al-Awal 1411 (2-3 December 1990).
5. 8th Annual Neurosciences, Riyadh Central Hospital, 27-28 Jumada Al-Thani 1411 (13-14 January 1991).
6. 6th Annual Paediatric Symposium, College of Medicine and King Khalid University Hospital, 26-27 Rajab 1411 (10-11 February 1991).
7. Gastroenterology and Hepatology, Security Forces Hospital, 10-11 Shaban 1411 (24-25 February 1991).
8. Postgraduate and Continuing Medical Education, College of Medicine and King Khalid University Hospital, 21-22 Shawwal 1411 (5-6 May 1991).

For further information, contact the Joint Board Office, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia; telephone (01) 467-1556 or 1564; telefax 481-1853; telex 403748 DARAYAH SJ.

King Saud University Hospitals Postgraduate Training Programs

King Saud University Hospitals (King Khalid University Hospital/King Abdul Aziz University Hospital) are pleased to invite applications for the following postgraduate training programs:

1. Arab Board residency training in the specialties of internal medicine, pediatrics, surgery, and obstetrics/gynecology.
2. Diploma courses in medical radiodiagnosis, laryngology/otology, psychiatry, and family practice.
3. Master's degree courses in pathology and family practice.
4. Residency training program in ophthalmology (in conjunction with King Khaled Eye Specialist Hospital).

For further information, contact the Director, Postgraduate Medical Education, College of Medicine, King Saud University, P. O. Box 2925, Riyadh 11461, Saudi Arabia.

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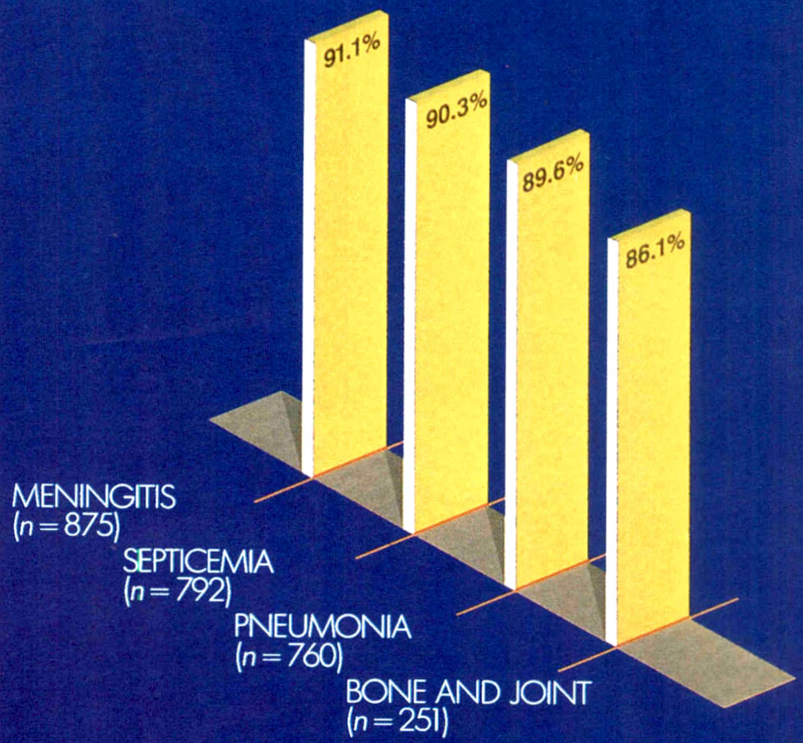

Components: Ceftriaxone. ***Indications:*** Sepsis; meningitis; abdominal infections; infections of the bones, joints, soft tissue, skin and of wounds; infections in patients with impaired defence mechanisms; renal and urinary tract infections; respiratory tract infections, particularly pneumonia, and ear, nose and throat infections; genital infections, including gonorrhea. Perioperative prophylaxis of infections. ***Dosage:*** Usual dosage for adults: 1–2 g once daily (every 24 hours). Further informations on administration and special dosage recommendations are available on request. ***Contr***
indications: Known hypersensitivity to cephalospori
Precautions: Pregnancy (particularly in the first trimeste
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(possibility of allergic cross-reactions). Anaphylactic shoc
Side effects: Gastrointestinal complaints. Hematologic
changes. Skin reactions. ***Packs:*** Packs for i.m. injection, 5
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IMPORTANT NOTICE The World Health Organisation (WHO*) has recommended that pregnant women and new mothers be informed of the benefits and superiority of breastfeeding – in particular the fact that it provides the best nutrition and protection from illness for babies.
Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle-feeding or other foods and drinks should be discouraged since it will have a negative effect on breastfeeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breast-feed.
Before advising a mother to use an infant formula, she should be advised of the social and financial implications of her decision: for example, if a baby is exclusively bottle-fed, more tha one can (450 g) per week will be needed, so the family circumstances and costs should be kep in mind. Mothers should be reminded that breast-milk is not only the best, but also the mos economical food for babies.
If a decision to use an infant formula is taken, it is important to give instruction on correct preparation methods, emphasizing that unboiled water, unboiled bottles or incorrect dilution can all lea to illness.

* See International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Res lution WHA 34.22, May 1981

Information for the medical profession only.

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THE EDITORS of the *Annals of Saudi Medicine* welcome contributions from our readers. The *Annals* will consider for publication manuscripts of interest to readers in Saudi Arabia, the Middle East, and around the world. All submissions are subject to review by the Editorial Board and by referees in appropriate specialties.

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فرجينيا جي كروزير
شيرلي موفيت

المدونات الطبية السعودية مجلة تنشر بموجب الأمر الملكي السامي رقم ٥/م/٢٤٢٢٣ بتاريخ ١٤ شوال عام ١٤٠٠هـ. وتصدر مرة كل شهرين، وهي مشروع مشترك بين كل من كلية الطب ومستشفى الملك خالد الجامعي ـ جامعة الملك سعود، صندوق بريد ٢٩٢٥ ـ الرياض ١١٤٦١، المملكة العربية السعودية، ومستشفى الملك فيصل التخصصي ومركز الأبحاث، صندوق بريد ٣٣٥٤ ـ الرياض ١١٢١١، المملكة العربية السعودية. يتم صف وطبع المجلة بمطابع جامعة الملك سعود. كل المراسلات والاستفسارات وطرق الحصول على المستلات ترسل إلى مكتب المطبوعات على العنوان التالي:

مكتب المطبوعات
مدونات الطب السعودي
مستشفى الملك فيصل التخصصي ومركز الأبحاث
ص.ب ٣٣٥٤
الرياض ١١٢١١ ـ المملكة العربية السعودية

منـدوب الاعلانـات
بي آر سي المتحدة
ابسوم ـ سري ـ المملكة المتحدة

الآراء التي ترد في المقالات المنشورة تعبر عن رأي أصحابها فقط ولا تعبر عن وجهة نظر مجلة المدونات الطبية السعودية. لا يسمح بإعادة طبع أي جزء من المجلة أو نسخه بأي شكل وبأي وسيلة سواء أكانت إليكترونية أو آلية، بما في ذلك التصوير والتسجيل أو الإدخال في أي نظام حفظ أو استعادة معلومات إليكتروني، بدون الحصول على موافقة مسبقة من إدارة المجلة.

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1. Proceedings of Int. Symp. Excerpta Medica 1984, 54-67.
2. Roy. Soc. Med. Int. Cong. and Symp. Series **80**, 173-180.

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Further information is available on request. BACTROBAN is a trademark.

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ANNALS
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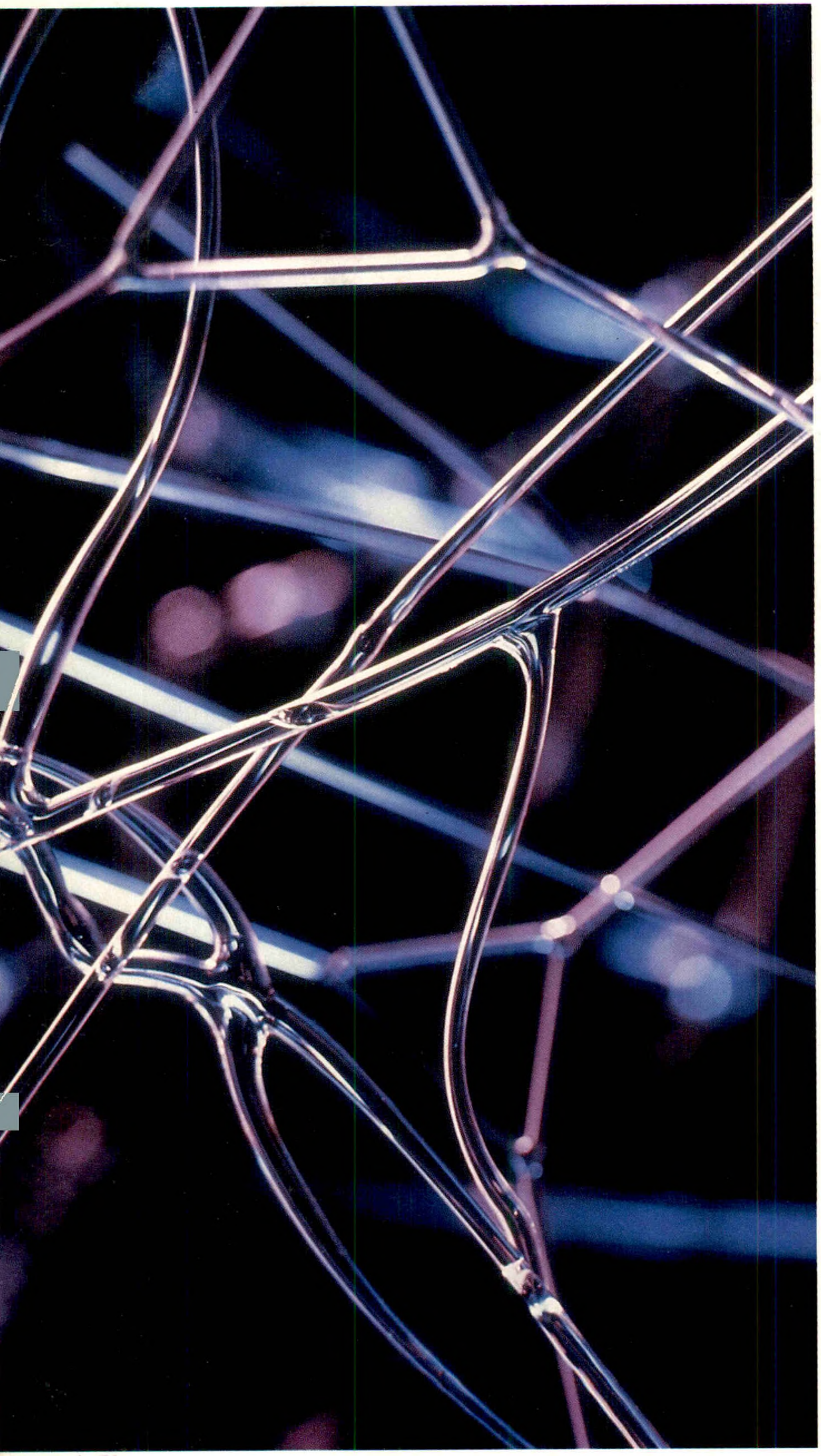
A BREAKTHROUGH IN CORONARY THROMBOLYSIS



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1. Van de Werf et al J Am Coll Cardiol 1988:12:14A-9A
2. TIMI Study Group N Engl J Med 1985:312 (14)932

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ANNALS OF SAUDI MEDICINE

Aims and Scope

The *Annals of Saudi Medicine* is a joint project of the King Faisal Specialist Hospital and Research Centre and the King Saud University College of Medicine and King Khalid University Hospital. The journal is typeset and printed at the King Saud University Press, Riyadh, Saudi Arabia. Since July 1985, the *Annals* has incorporated *The King Faisal Specialist Hospital Medical Journal*, established in 1980.

The *Annals* is a bimonthly multidisciplinary medical journal. High-quality papers, written in English, dealing with aspects of clinical, academic or investigative medicine or research will be welcome. Emphasis is placed on matters relating to medicine in Saudi Arabia in particular, and the Middle East in general, though articles are welcome from anywhere in the world, and the *Annals* has worldwide readership.

The *Annals* publishes original articles, case reports, letters to the editor, editorials, and from time to time, special communications, commentaries, and review articles. Abstracts of meetings and symposia sponsored by the Joint Board for Postgraduate Medical Education of Saudi Arabia are published, and the proceedings of such symposia may be published if the Editorial Board considers them appropriate and relevant. The Editorial Board wishes to minimize delay between manuscript submission, decision, and publication, and accordingly authors are requested to follow carefully the instructions set out under "Information for Authors."

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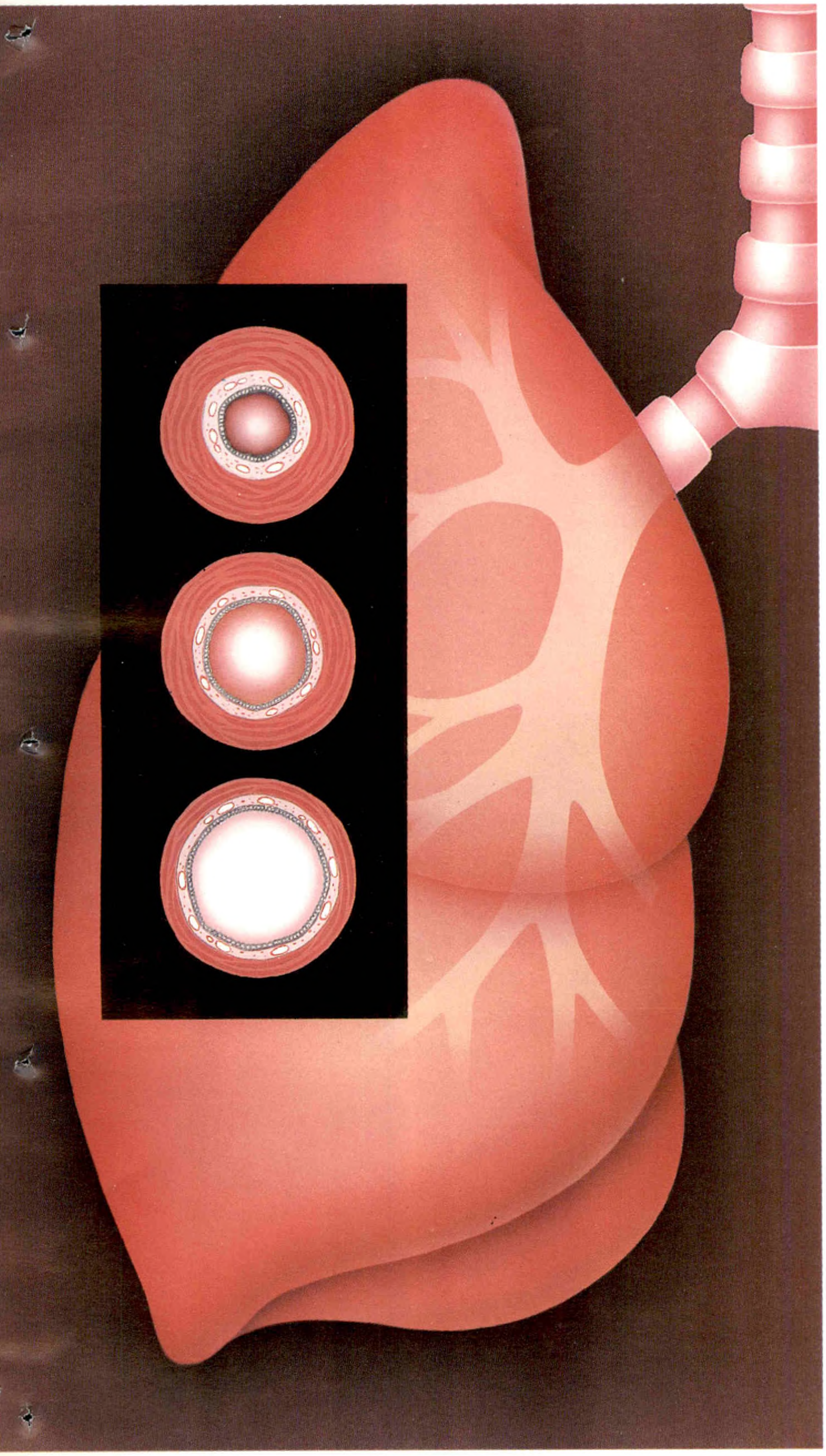

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1. Gold W Postgrad Med J 1975:51 (Suppl 7)
2. Nadel JA New Dimensions in the Management of Airways Disease and Rhinitis. Auckland: ADIS Press 1982.
3. Tashkin DP. Am J Med 1986:81 (Suppl 5A) 81-90
4. MacVicar J et al. New Dimensions in the Management of Airways disease and Rhinitis. Auckland: ADIS Press 1982.

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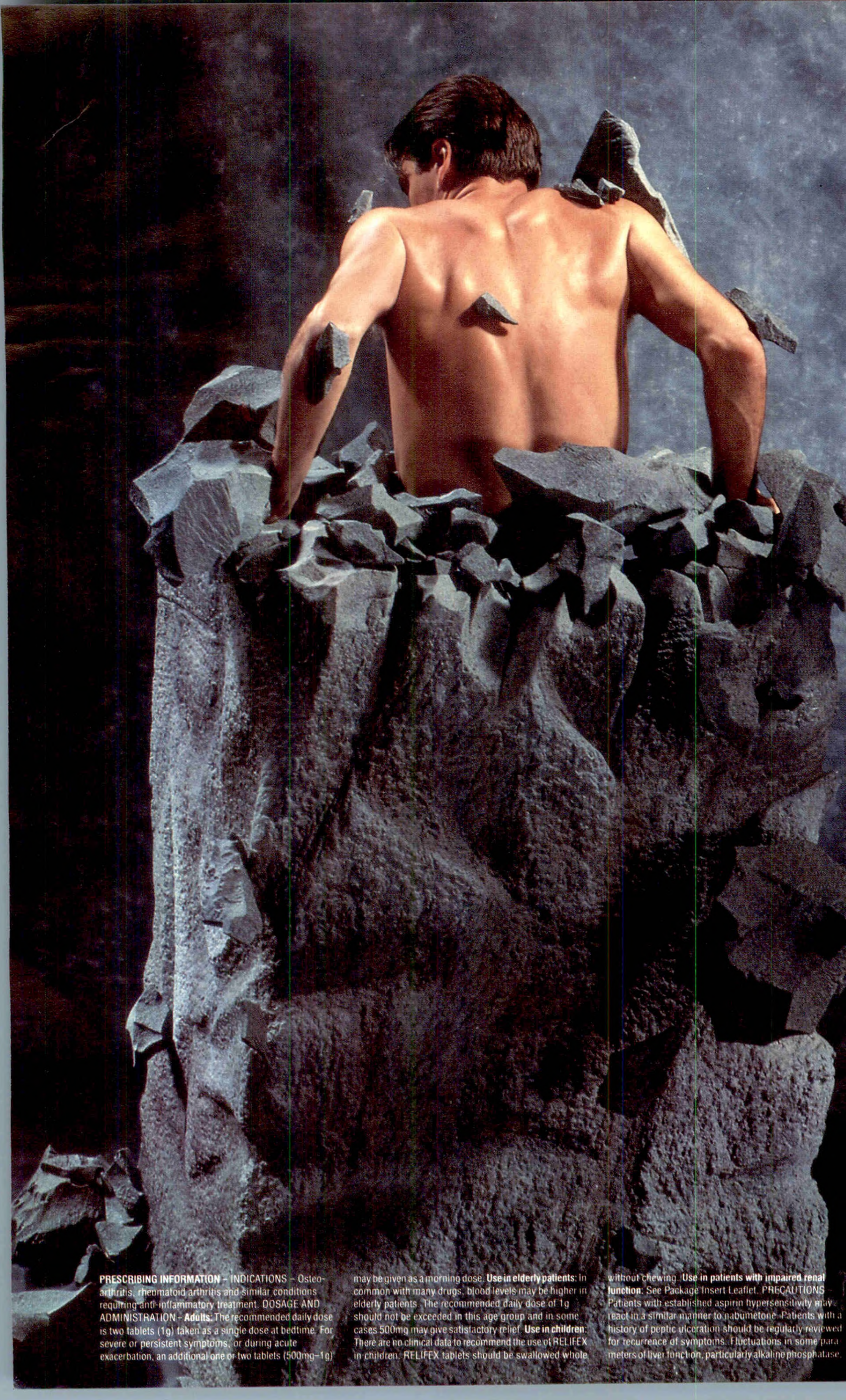

PRESCRIBING INFORMATION – INDICATIONS – Osteoarthritis, rheumatoid arthritis and similar conditions requiring anti-inflammatory treatment. DOSAGE AND ADMINISTRATION – **Adults:** The recommended daily dose is two tablets (1g) taken as a single dose at bedtime. For severe or persistent symptoms, or during acute exacerbation, an additional one or two tablets (500mg–1g) may be given as a morning dose. **Use in elderly patients**: In common with many drugs, blood levels may be higher in elderly patients. The recommended daily dose of 1g should not be exceeded in this age group and in some cases 500mg may give satisfactory relief. **Use in children**: There are no clinical data to recommend the use of RELIFEX in children. RELIFEX tablets should be swallowed whole without chewing. **Use in patients with impaired renal function**: See Package Insert Leaflet. PRECAUTIONS – Patients with established aspirin hypersensitivity may react in a similar manner to nabumetone. Patients with a history of peptic ulceration should be regularly reviewed for recurrence of symptoms. Fluctuations in some parameters of liver function, particularly alkaline phosphatase,

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nabumetone

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y observed in patients with chronic inflam-
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these changes. CONTRA-INDICATIONS –
ulceration, severe hepatic impairment (e.g.
abumetone hypersensitivity. SIDE EFFECTS –
include diarrhoea, dyspepsia, nausea,
, abdominal pain, flatulence, headache,

dizziness, pruritus, rash and sedation. In clinical trials, increases in dose above 1g did not lead to an increase in the incidence of side effects. AVAILABILITY – RELIFEX tablets: Red, film coated tablets marked RELIFEX on one side and 500 on the other side. Each tablet contains 500mg nabumetone.

REFERENCES: 1. Roth SH, *Am J Med* 1987; **83** (Suppl 4B): 25–30. 2. Appelrouth DJ *et al*, *Am J Med* 1987; **83** (Suppl 4B): 78–81. 3. Carle WK, Rotman H, *R Soc Med Int Congr Symp Ser* 1985; (69): 139–148. 4. Brobyn RD, *Am J Med* 1987; **83** (Suppl 4B): 50–54.

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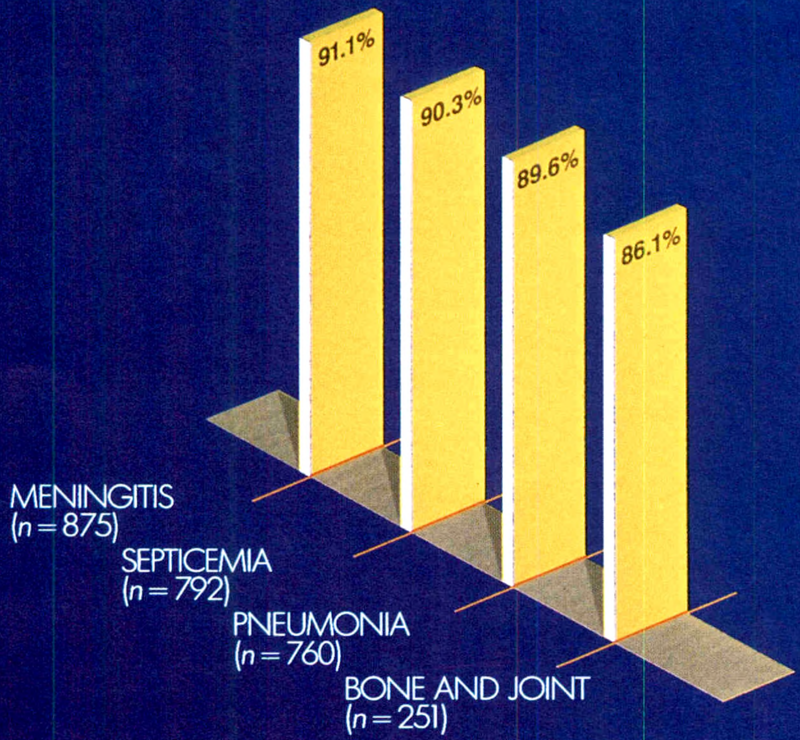

Components: Ceftriaxone. ***Indications:*** Sepsis; meningitis; abdominal infections; infections of the bones, joints, soft tissue, skin and of wounds; infections in patients with impaired defence mechanisms; renal and urinary tract infections; respiratory tract infections, particularly pneumonia, and ear, nose and throat infections; genital infections, including gonorrhea. Perioperative prophylaxis of infections. ***Dosage:*** Usual dosage for adults: 1–2 g once daily (every 24 hours). Further informations on administration and special dosage recommendations are available on request. ***Contra-indications:*** Known hypersensitivity to cephalosporins. ***Precautions:*** Pregnancy (particularly in the first trimester) unless absolutely necessary. Hypersensitivity to penicillin (possibility of allergic cross-reactions). Anaphylactic shock. ***Side effects:*** Gastrointestinal complaints. Hematological changes. Skin reactions. ***Packs:*** Packs for i.m. injection, 5's. Packs for i.v. injection, 5's. Packs for i.v. infusion, 5's. Full details are available on request.

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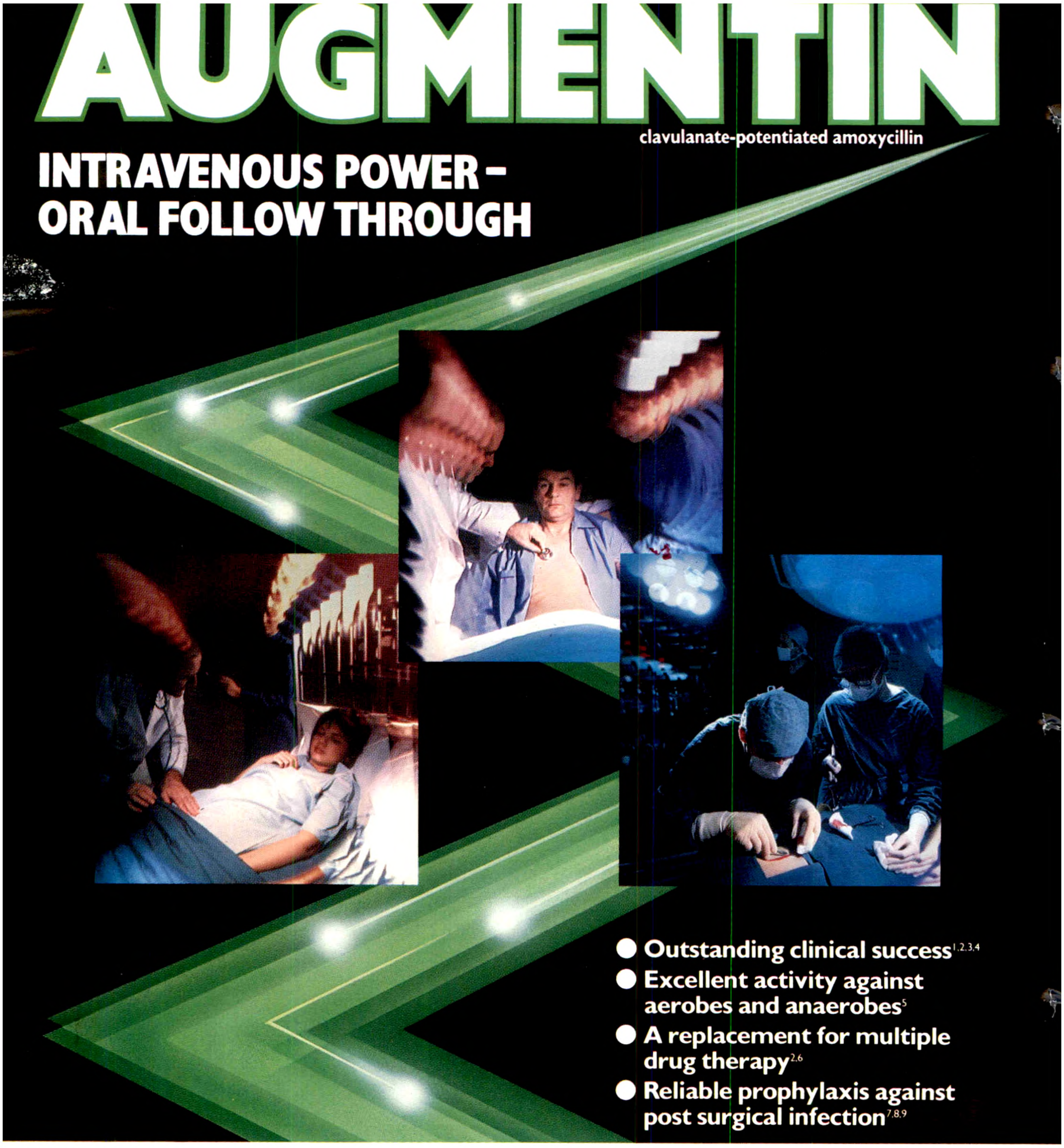

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escribing Information

dications: Upper/lower respiratory tract infections: sinusitis, tonsillitis, otitis media,
ite and chronic bronchitis, pneumonia, empyema, lung abscess. Skin and soft tissue
ections: Boils/abscesses, cellulitis, wound infections, intra-abdominal sepsis. Genito-
nary tract infections: cystitis, urethritis, pyelonephritis, septic abortion, pelvic
ections, chancroid, gonorrhoea. Osteomyelitis, septicaemia, peritonitis, surgical
phylaxis.
al dosage: Adults and children over 12 years: One tablet tds. Children 7-12 years:
ml of 156mg syrup. Children 2-7 years: 5ml of 156mg syrup. Children
onths-2 years: 2.5ml of 156mg syrup. Children below 9 months: No suitable
sentation currently available. In severe infections the dosage may be doubled.
ravenous dosage: Adults and children over 12 years 1.2g 6-8 hourly. Children
onths-12 years 30mg/kg 6-8 hourly. Children below 3 months see pack insert leaflet.
gical prophylaxis: Adults: 1.2g at induction of anaesthesia. Procedures longer than
our require subsequent doses (up to 4 in 24 hours). Treatment with AUGMENTIN
uld not be extended beyond 14 days without review.
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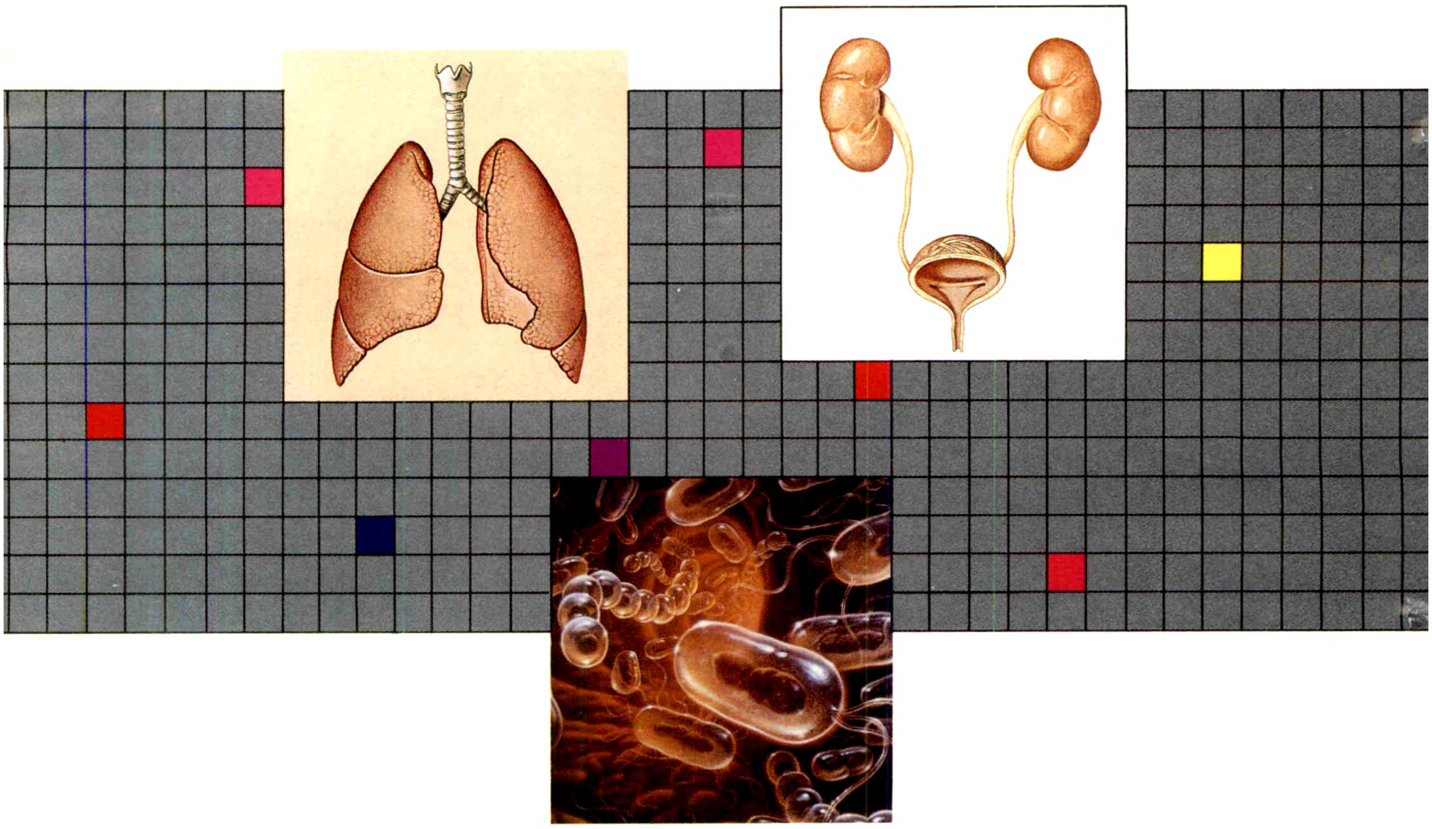

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Editorial

THE ACT OF DYING IS ONE OF THE ACTS OF LIFE

The quotation "the act of dying is one of the acts of life" from Marcus Aurelius expresses the philosophy involved in cadaveric organ transplantation. In this issue of the *Annals of Saudi Medicine* we publish an article on this subject as observed in Saudi Arabia.[1] In this interesting article, the author points out that on a worldwide basis there are some 55 potential organ donors per million population, but here in the Kingdom of Saudi Arabia organs from only 4 or 5% of potential donors are currently being utilized.

However, the whole concept of transplantation of organs from the dead is quite new in this country, and there is evidence that, as people become aware of the potential benefits of organ donation, the number of cadaveric transplants is increasing. Thus, at one major institution in Riyadh the number of kidney transplants doubled in two years, and during the past year or so there have been several heart transplants in Riyadh, with plans well advanced for liver transplantation.

Attitudes toward death and what can or cannot be done with a dead body are conservative in this predominantly Muslim community. As was pointed out with regard to the growing need for a greater number of autopsies,[2] it must be remembered that it is only within the past two decades that modern and increasingly sophisticated medicine has been introduced to Saudi Arabia. So it is still comparatively early for the development of positive attitudes toward transplantation of organs from the cadaver.

Just as the Quran does not prohibit autopsies but does require the greatest of respect for the dead body, so also is it permissible to remove an organ or part thereof from a Muslim for transplantation, provided the removal causes no dissatisfaction and the transplantation seems likely to be successful. This was confirmed by Senior Muslim Religious Leaders in 1982 (See Ref. 1, Appendix A).

One problem that continues to exercise religious, legal, medical, and scientific minds throughout the world concerns the definition of death—for of course the sooner an organ is removed from a dead body, the more likely is it to be successfully grafted into the recipient. Brain death is usually the critical event that allows attending physicians to pronounce death, and this can be decided by objective scientific means. Again, this important matter has been addressed by the Council of Islamic Jurisprudence (see Ref. 1, Appendix B).

The type of patient who meets the criteria for organ donation very often is one dying in tragic circumstances. Commonly, it is a previously fit and healthy young adult who has been involved in an accident, often a motor vehicle accident. The relatives of such a patient are of course living through a most stressful and unexpected event, and it is not easy for them or for those seeking organs for transplantation to deal with a request for organ donation. Yet the request cannot be delayed until much after death, for then the organs are unsuitable. But it is remarkable and wonderful how so many relatives react positively to a well-explained and sensitively presented request for organ donation. The main point should always be that, given the tragic impending death, the possibility of the dying person being able to help relieve the illness and suffering of another human being is a ray of hope in an otherwise depressing scene. Just as autopsies allow others to learn from an individual's death, so do organ donations allow one to gain at least something from death—to make the best of a bad job.

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Original Articles

PAPILLEDEMA WITHOUT LATERALIZING SIGNS

Tahir Obeid, MRCP(UK); Chrysostomos P. Panayiotopoulos, MD, PhD;
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Abdul Kader Daif, MD

أجريت دراسة مراجعة لأربعين مريضًا (تتراوح أعمارهم بين ١٨ ـ ٤٠ سنة) يعانون من وذمة الحليمة البصرية بدون علامات شِقّية مع تركيز خاص على أسبابها الخفية. كان كل من فرط الضغط الحميد داخل القحف وورم المخ الكاذب من أكثر الأسباب انتشارًا، تلاهما تخثر جيوب الجافية. وكان فرط الضغط الحميد داخل القحف أكثر انتشارًا بين النساء (٢٥ أنثى مقابل ذكر واحد) بينما كان تخثر جيوب الجافية أكثر انتشارًا بين الرجال (سبعة ذكور مقابل إثنين). وكانت الآفات الكتلية أقل الأسباب شيوعًا. إن الذكور الذين يعانون من وذمة الحليمة البصرية بدون علامات شقية، والإناث اللواتي لا يحملن العوامل المؤهبة لفرط الضغط الحميد داخل القحف يجب أن يجرى لهم تصوير الأوعية بجهاز طرح الظلال الرقمي وأن تجري متابعتهم بصورة منتظمة لاستبعاد اصابتهم بأي خلل بنيوي خفي قبل تشخيص حالاتهم على أنها فرط ضغط حميد داخل القحف.

The cases of 40 patients (aged, 18-40 y) who presented with papilledema without lateralizing signs (PWLS) were analyzed retrospectively, with particular reference to the underlying causes. Benign intracranial hypertension and pseudotumor cerebri were the most common causes and dural sinus thrombosis was the next most common. Benign intracranial hypertension was more prevalent among women (25 females versus one male) and dural sinus thrombosis was more prevalent among men (seven males versus two females). Space-occupying lesions were the least common cause. Males presenting with PWLS and females lacking the risk factors for benign intracranial hypertension should undergo digital subtraction angiography and be followed regularly to rule out any underlying structural disorder before a diagnosis of benign intracerebral hypertension can be made.

Papilledema is a swelling of the optic nerve head due to raised intracranial pressure.[1] Before the introduction of modern imaging techniques, 60% of patients with intracranial brain tumors were reported to have papilledema,[2] although this figure has decreased to 25% because of earlier diagnosis and better overall management.[3] In a review of 238 patients with PWLS published 33 years ago,[4] it was reported that 45% had lateralized mass lesions, 26% had obstructive midline lesions, and only 11% had benign intracranial hypertension (BIH), revealed by air encephalography and surgical exploration. Twenty years later, Weisberg[5] evaluated PWLS in 100 patients and found that the earlier figures had reversed (BIH, 71%; mass lesions, 18%; heterogeneous causes, 11%). We have been unable to find a comparative study done in the context of modern imaging techniques and published since Weisberg's report. Furthermore, BIH may be erroneously diagnosed in patients if they have undergone only computed tomographic (CT) screening but not angiography and if no regular follow-up has been done. The diagnosis of BIH should only be made in patients with raised intracranial pressure, a CT scan demonstrating normal or slit-like ventricles, normal cerebrospi-

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nal fluid findings, and the presence of widely associated and recognized risk factors detected after a regular follow-up.

Methods

The cases of 44 adults with papilledema without lateralizing signs (PWLS) investigated in the Neurology Division of King Khalid University Hospital between December 1983 and December 1987 were analyzed retrospectively. There were nine males and 31 females. Patients with lateralizing neurological signs, meningeal irritation, or a history of head trauma were excluded. All patients had been followed for at least 6 months.

All patients had routine blood and urine biochemical assessment profiles. They also had had CT brain scans, and lumbar puncture was performed in all but five, four of whom were excluded because they refused the procedure and therefore a definitive diagnosis was not reached. CT scanning demonstrated brain tumors in two patients and a hemorrhagic infarct in a third. Digital subtraction angiography (DSA) was carried out in all nine males and in 14 females, and two patients had fluoroscein angiography of the retina to confirm the presence of nerve head swelling.

Results

A definite diagnosis was made in 40 patients. BIH was the final diagnosis in 26 (65%), DST in nine (22.5%), and intracranial tumors in two patients (one colloid cyst of the third ventricle and one sphenoid wing meningioma). Three patients (7.5%) suffered from chronic meningitis, two with *Brucella* and one with tuberculous meningitis (Table 1). These patients did not have overt clinical signs of meningeal irritation.

BIH was more prevalent in women (25 females versus one male) whereas DST was more prevalent in men (seven males versus two females). The average ages of the two groups were 26 years and 33 years, respectively. The one male with a diagnosis of BIH was on hormonal therapy prescribed for infertility, the nature of which was not known.

TABLE 1. *Final diagnosis.*

Etiology	No.	%	Males	Females
Benign intracranial hypertension	26	65.0%	1	25
Dural sinus thrombosis	9	22.5%	7	2
Chronic bacterial meningitis	3	7.5%	–	3
Brain tumor	2	5.0%	1	1

Symptoms were essentially the same in all patients. Headache occurred in all patients and visual disturbances were the next most common complaint. Two patients with DST suffered convulsions. The recognized risk factors were present in most of the female patients with BIH. Obesity was seen in 11 cases, birth control pill use in eight, menstrual disturbances in four, pregnancy in one, and infertility and hormonal therapy in one (the only male affected by BIH). No predisposing risk factors were seen in six patients. A cause was found in all but one patient with DST (Table 2). A misdiagnosis of BIH was rendered initially in patients 2 through 4 who were later shown to have Behcet's syndrome. Patient 5, whose symptoms also resembled BIH, was later found to have a sarcoma of the occiput.

Patients with BIH were treated by repeated lumbar puncture and/or corticosteroids. Serious visual deterioration did not develop in any of these patients during a follow-up period that averaged 9 months. Patients with DST were treated with corticosteroids and long-term anticoagulation and one patient had a lumboperitoneal shunt installed. Two patients died, one with malignant melanoma and one with sarcoma of the occiput. One patient became blind because of subsequent optic atrophy, and the course in the six remaining patients was uneventful though long-term follow-up was not possible. Two patients with chronic *Brucella* meningitis recovered completely following treatment with doxycycline and co-trimoxazole. The patient who suffered from chronic tuberculous meningitis also recovered satisfactorily with antituberculous drugs.

Discussion

Before the advent of CT scanning of the brain, PWLS was believed to be caused by lateralized or midline obstructive lesions.[6-8] Weisberg[5] found that 18% of the 100 patients with PWLS in his study had brain tumors; 71% were due to BIH and the remaining 11% had "miscellaneous" causes. In our study, BIH was the most common cause

TABLE 2. *Etiology of dural sinus thrombosis.*

No. of cases	Age(y)	Sex	CT	CSF composition	Etiology
1	24	M	Normal	Abnormal	Behcet's disease
2	26	M	Normal	Normal	Behcet's disease
3	25	M	Normal	Normal	Behcet's disease
4	40	M	Normal	Normal	Behcet's disease
5	43	M	Normal*	Normal	Sarcoma of the occiput
6	33	M	Empty delta sign	Normal	Unknown
7	32	F	Normal	Normal	Malignant melanoma of the axilla
8	32	F	Normal*	Normal*	Systemic lupus erythematosus
9	33	F	Venous infarct	Not done	Pregnancy

*Abnormal on follow-up.
M = male; F = female; CT = computed tomography; CSF = cerebrospinal fluid.

(65%) followed by DST (22.5%). Brain tumors were the least common (5%). BIH was 25 times more common in females than males, whereas most cases of DST occurred in males. Earlier reports[9,10] have suggested that DST was more common in females and the elderly, although Bousser et al[11] found no sex difference. Our patients were highly selected and were not representative of the spectrum of DST.[12-17] Initial evaluation in some patients with DST suggested BIH, but reassessment and the use of DSA revealed more serious underlying pathology, notably Behcet's syndrome and sarcoma of the occiput. To avoid incorrect diagnosis of BIH, we suggest that all male patients and any female patients lacking the risk factors for BIH[18-20] should be screened with DSA and MRI, which has recently been found to be of potential value in diagnosing DST.[21,22] These patients should be followed for long enough so that other and more serious possibilities can be excluded. BIH encompasses a diverse group of nosological entities and its pathophysiology remains obscure.[23] However, the fundamental principles of management in BIH and DST are the same. Long-term anticoagulant therapy is of dubious value in DST, although it may have been useful in some of our patients, a view supported by Bousser et al.[11] However, clinical and neuroradiological follow-up in our patients was not sufficient to establish the value of anticoagulation. The natural history of BIH is usually benign.[18-20] This differs from DST which has an unpredictable prognosis and with a reported mortality that varies from 10 to 15%[11] depending on the cause and extent of the thrombosis. In the present study, two patients with chronic *Brucella* meningitis exhibited PWLS with normal radiological findings. Papilledema as a presenting manifestation of neurobrucellosis has rarely been reported.[24,25] In areas where the condition is endemic, it should be included in the differential diagnosis of PWLS especially because of its excellent response to chemotherapy.

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DUODENAL ULCERS IN THE EASTERN REGION OF SAUDI ARABIA

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أجرينا دراسة لتحديد نسبة إفراز الحمض المعدي لدى ٣٦ شخصاً يشكلون مجموعة ضبط (٢٥ ذكرًا و ١١ أنثى) و ٥٨ مريضًا مصابين بقرحة عفجية (٤٤ ذكرًا و ١٤ أنثى) باستخدام طريقة تتناول تصحيح حالات فقد البواب والجزْر العفجي المعدي. وكانت معظم حالات الدراسة من السعوديين باستثناء تسعة مواطنين يمنيين. بلغ متوسط إفراز الحمض القاعدي وإفراز الحمض المستحث بالبنتاغسترين أ؛ و النتاج الأقصى للحمض في الذكور من مجموعة الضبط ١,٧٨ ± ١,٤٩ (SD) و ١٩,٨٦ ± ٧,٩١ مليمول/س. على التوالي. كما بلغت القيم المقابلة لدى الاناث من مجموعة الضبط ١,٧٦ ± ٢,٠٢ و ١٦,٢٣ ± ٤,٣٣ مليمول/س، وكان ترابط النتاج الأقصى من الحمض إيجابيًا مع الطول والوزن وكتلة الجسم خلا الدهون (LBM)، وسلبيًا مع السن. أما في مجموعة المصابين بقرحة العفج، فقد بلغ متوسط افراز الحمض القاعدي نتاجه الأقصى لدى الذكور ٣,٨١ ± ٣,٤٢ و ٢٧,٠٨ ± ٩,٥٤ مليمول/س، ولدى الاناث ١,٥٥ ± ٢,٣٧ و ١٨,٦٠ ± ٧,٥٣ مليمول/س. كان ترابط النتاج الأقصى للحمض إيجابيًا مع الطول، والوزن، وكتلة الجسم خلا الدهون (LBM)، ومدة المرض. كان متوسط افراز الحمض القاعدي والمستحث أعلى بدرجة هامة في الذكور المصابين بقرحة العفج بالمقارنة مع الذكور من مجموعة الضبط، وكانت نسبة مفرطي الافراز ٢٠,٤٥٪. أما في الاناث فكانت هذه النسبة عند الحد الفاصل. , كانت نسبة إفراز الحمض لدى الرجال أكثر منها لدى النساء، وعند معايرة النتاج الأقصى نسبة إلى الطول اختفى هذا الفارق الجنسي. كما أن المعايرة بالنسبة إلى الطول لم تؤثر على الفروق في نسب افراز الحمض بين المرضى المصابين بقرحة عفجية ومجموعة مرضى الضبط. أكدت نتائج دراستنا العلاقة المعروفة لزمرة الدم (O) بالقرحة العفجية وأظهرت العلاقة المهمة لهذا المرض بالتاريخ الأسري للقرحة الهضمية. كذلك كانت نسبة المدخنين بين المرضى الذكور المصابين بالقرحة العفجية أعلى، بدرجة هامة، منها بين الذكور من مجموعة الضبط. ومع أنه لم يلاحظ أن التدخين المزمن يزيد من نسبة إفراز الحمض لدى الذكور المصابين بقرحة عفجية، إلا أن ذلك لوحظ لدى الذكور من مجموعة الضبط. هذه النتيجة تأكدت بعد المعايرة نسبة إلى الطول بوجود ترابط إيجابي بين معالم إفراز الحمض المعدي وعدد السجائر المستهلكة يوميًا وسنوات التدخين.

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Using a method that involves corrections for pyloric losses and duodenogastric reflux, we determined gastric acid secretion in 36 control subjects (25 males and 11 females) and 58 patients with duodenal ulcer (44 males and 14 females). Most of the study subjects were Saudis, except for nine Yemenis. Mean basal and pentagastrin-stimulated or maximal acid outputs in male controls were 1.78 ± 1.49 (SD) and 19.86 ± 7.91 mmol/h, respectively; in female controls the corresponding values were 1.76 ± 2.02 and 16.23 ± 4.33 mmol/h, with maximal secretion positively correlating with height, weight, and lean body mass (LBM), and negatively with age. In the duodenal ulcer group, mean basal and maximal acid outputs for men were 3.81 ± 3.42 and 27.08 ± 9.54 mmol/h and for women, 1.55 ± 2.37 and 18.60 ± 7.53 mmol/h. Maximal acid secretion correlated positively with height, weight, LBM, and duration of illness. In male patients with duodenal ulcer, mean basal and stimulated acid secretion were significantly higher than in the male controls, the proportion of hypersecretors being 20.45%. In women the differences were of borderline significance. Men secreted more acid than women, and when maximal secretion was standardized for height, this sex difference disappeared. Height standardization did not affect the differences in acid secretion between patients with duodenal ulcer and controls. Our results confirmed the well-known association of blood group O with duodenal ulcer and revealed a significant association of this disease with family history of peptic ulcer. The prevalence of smoking is significantly higher among male patients with duodenal ulcer than among male control subjects. Although chronic cigarette smoking was not observed to elevate acid secretion in male patients with duodenal ulcer, it was observed in the male control subjects. This finding was confirmed after height standardization by positive correlation of gastric acid secretion parameters with the number of cigarettes smoked per day and the duration of the habit in years

Duodenal ulcer disease is a heterogeneous disorder resulting from the interaction of both genetic and environmental factors. It also has a complex pathophysiology, a prominent feature of which is gastric acid hypersecretion.[1] Hereditary indicators include a family history of peptic ulcer and association with blood group O.[2] An important environmental factor is cigarette smoking.[3]

The extent of gastric acid hypersecretion in response to pentagastrin or histamine observed in duodenal ulcer patients compared to controls is associated with ethnic and geographic variables. The percentage of duodenal ulcer patients secreting acid maximally above the upper limit varies from 16 to 56% in countries ranging from the U.S.A. with the lowest percentage, to Africa, India, Hong Kong, and the U.K. with the highest percentage.[2] Chronic smoking has been shown to elevate gastric acid secretion.[4-7]

The purpose of the present study was to define the pattern of gastric acid secretion in Saudi patients with duodenal ulcer compared to healthy control subjects, and to relate gastric acid secretion to a family history of peptic ulcer and to blood group. We also evaluated the association of smoking with duodenal ulcer disease and the effect of chronic smoking on gastric acid secretion in our Saudi population. The outcome points up the need for a greater awareness of smoking as an environmental hazard, especially in the Kingdom of Saudi Arabia where cigarette smoking seems to be prevalent and relatively free of the restrictions that have been adopted in most developed countries.

Subjects and Methods

Fifty-eight patients with duodenal ulcer (44 males and 14 females) diagnosed by endoscopy were studied. The control group consisted of 25 males and 11 females. They were mainly hospital patients without either upper gastrointestinal symptoms or diseases known or believed to affect gastric secretion. A few were healthy volunteers. All subjects were Saudis except for five control subjects and four patients with duodenal ulcer who were from Yemen.

The method of measurement of gastric acid secretion used in this study is one of the most accurate and includes refinements in the gastric aspiration technique that allow correction of the gastric aspirate for pyloric losses and duodenogastric reflux.[8]

The procedure is as follows. All medication was stopped 3 to 7 days before the test and the subject reported to the laboratory at about 8 AM, after fasting for 12 hours. Patient height and weight were measured, from which lean body mass (LBM) was later calculated using Hume's formula. A double-lumen nasogastric tube was passed into the stomach and its position ascertained by the water recovery test.[9] Full information was then obtained from the subject, including family history of peptic ulcer and questioning about smoking. The information was entered into a computer-compatible data sheet.

Ex-smokers were considered as smokers. None of the females smoked, so all smokers were male. The smoking factor (SMF) was calculated by obtaining the square root of No. of years of smoking × No. of cigarettes smoked per day. Obtaining the square root ensured normal distribution. Only three subjects preferred smoking sheesha (hubble-bubble) to cigarettes (two controls and one patient with duodenal ulcer).

Blood was withdrawn for determination of blood group and a saline drip was set up. The marker phenolphthalein (PSP) was infused through the thin nasogastric tube into the stomach and gastric contents were collected by an automatic gastric suction pump (Sycopel Scientific Ltd., U.K.) every 10 minutes. After basal collection for one hour, pentagastrin (Peptavlon, ICI) was infused intravenously using an Orion infusion pump (model M352; Orion Research Inc., U.S.) at 6 μg/kg/h and samples collected for about 1½ to 2 h to obtain a plateau of secretion from which maximal secretion could be calculated. Each sample was automatically titrated using an automated titration system with an autoburette (Radiometer A/S, Denmark) until a pH of 7.0 was reached. Na^+, K^+, and Cl^- concentrations were determined on a Nova 5 electrolyte analyzer (Nova Biochemical, U.S.), while the absorbance of PSP was determined on an LKB spectrophotometer (LKB Producter AB, Sweden).

All the data were fed into the King Faisal University mainframe computer using an interactive program. This program calculated all the required gastric secretion parameters for the basal period and for the stimulated period after objectively selecting the plateau. The basis of the calculations to obtain the corrected volumes and outputs and for selecting the plateau were given in the paper by Whitfield and Hobsley;[8] only the main points are highlighted here.

Correction of secretion volumes was achieved using an artificial marker (PSP), which is neither destroyed nor absorbed in the stomach, and by a natural marker—Na^+. Since Na^+ concentration in pure gastric juice is low and constant at 7 mmol/L while in duodenal juice it is about 150 mmol/L, reflux of duodenal contents into the stomach can be estimated by a formula based on Na^+ output in the stomach. No precaution against, or correction for, swallowed saliva was attempted.

Using the dilution principle, the total gastric contents per 10 minutes (V_{tot}) can be calculated after spectrophotometric determination of PSP in standard and sample.

Since 1.7 ml of PSP solution is infused into the stomach every 10 minutes, V_{tot} can be corrected to give V_{cor}, i.e. $V_{tot} - 1.7$ ml.

The aspirated volume (V_{asp}) can be corrected to give the observed volume (V_{obs}) by subtracting the fraction of PSP recovered volume as follows: $V_{obs} = V_{asp} - (1.7 \text{ ml} \times V_{asp}/V_{tot})$.

Correction for the volume refluxed from the duodenum into the stomach is done by calculation of the volume refluxed (V_r) using the following formula[10]: $V_r = 7.34\ QNa - 0.0712\ V_{cor} - 1.281$, where QNa is the sodium output of the respective volume in millimoles per 10 minutes.

Subtraction of V_r from V_{cor} yields V_g which is the volume corrected both for pyloric losses and duodenogastric reflux: $V_g = V_{cor} - V_r$.

Acid output in mmol/h = $V_{obs} \times [H^+]$ in mmol/L × 0.006.

Our results are given for both the basal and stimulated periods as acid output, V_{obs} and V_g per hour.

Statistical Analysis

Results are generally reported as the mean ($\bar{X}$) and standard deviation (SD). Differences between sample means in two independent samples (e.g., duodenal ulcer patients versus controls for the same sex) were assessed by Student's *t* test; two techniques for equal and unequal variances were employed as appropriate.

Differences between proportions were assessed by the chi-square or Fisher's exact test, as appropriate.

Linear correlations of variables of gastric secretion versus indices of body size, age, smoking factor, or duration of illness were investigated by simple regression and by multiple regression; in all cases the P value for analysis of variance (ANOVA) test of linearity was calculated. Two approaches were used to select the best multiple regression equation, namely, forward selection and stepwise regression. Significance level for entering the regression equation was set at 0.2. If P was less than 0.05, the result was considered significant; if $0.05 < P$ value < 0.1, the result was considered suggestive; and if P was greater than 0.1, the result was not significant.

We used the method of Maybury et al[11] to standardize gastric secretion to the mean height of the group, rather than dividing gastric secretion by height. All statistical computations were done on the IBM mainframe computer at King Fahd Hospital of the University at Al-Khobar using the Statistical Analysis System.

Results

Table 1 summarizes the body size variables, blood group distribution, family history of peptic ulcer, and prevalence of smoking in control subjects and patients with duodenal ulcer, subdivided according to sex. While ages and weights were comparable, the female subjects were shorter and had a lower LBM than did the male subjects in both the control and duodenal ulcer groups.

TABLE 1. *Summary of body size variables, blood group distribution, family history of peptic ulcer, and prevalence of smoking in control subjects and patients with duodenal ulcer.*

	Control		Duodenal Ulcer	
	Male	Female	Male	Female
Numbers	25	11	44	14
Mean age (y) ± SD	31.80± 12.53	34.09 ± 12.52	34.43± 11.00	38.21 ± 11.98
Mean weight (kg) ± SD	65.52± 15.10	58.45 ± 15.72	61.09± 9.85	62.36 ± 15.17
Mean height (cm) ± SD	165.32± 5.36	152.73*± 7.80	164.48± 5.93	153.57*± 5.12
Mean LBM (kg) ± SD	48.05± 5.86	38.41*± 4.93	46.54± 4.48	39.36*± 5.55
No. of subjects by blood group				
A	10	5	11	4
B	3	5	6	1
AB	3	–	3	–
O	9	1	24	9††
Number with family history of peptic ulcer	–	1	7†	2
Nonsmokers	17	11	18	14
Smokers				
Cigarettes	6	–	25†	–
Sheesha	2	–	1	–
Total	8	–	26†	–

* For $P = 0.0001$ when comparing between the sexes within the control or duodenal ulcer group by Student's t test.

† For $P < 0.05$ and †† for $P < 0.01$ when comparing duodenal ulcer patients with the control group for the same sex by Fisher's exact test or chi-square test, as appropriate.

LBM = lean body mass.

There was a higher frequency of group O over the other blood groups among the female patients with duodenal ulcer compared with the female controls. The increased number of male patients with duodenal ulcer with a family history of peptic ulcer compared to male controls was also significant. There were significantly more smokers among the male duodenal ulcer patients compared to male controls, regardless of inclusion or omission of the sheesha smokers.

Gastric acid secretion variables in the two main groups of subjects divided according to sex are given in Table 2. Within the control group, men were noted to secrete significantly more gastric acid than did women with regard to stimulated V_{obs} and V_g, while the differences in basal V_{obs} and stimulated acid output were of borderline significance. In the duodenal ulcer group, the sex difference is significant for both basal and stimulated acid output and suggestive for stimulated V_{obs}. When duodenal ulcer patients were compared with controls of the same sex, male patients were found to secrete significantly more gastric acid than did male controls with regard to basal and stimulated acid output and stimulated V_{obs}; significance was suggestive for basal V_g. Among female duodenal ulcer patients, there was a suggestive increase in basal V_g and stimulated V_{obs} and V_g.

Correlations of maximal acid secretion variables with indices of body build, age, and smoking factor, and for duodenal ulcer with duration of illness, were computed by both simple and multiple regressions. In control subjects, maximal acid secretion parameters correlated positively with height, LBM, and weight, and there was suggestive evidence *($P =$ 0.096)* of negative correlation with age. Smoking factor emerged as a positive factor in one of the valid multiple regression models. In patients with duodenal ulcers, maximal gastric acid secretion variables correlated positively with height, LBM, weight, age, and duration of illness. The strongest and most consistent correlations were with height in both the control and duodenal ulcer groups.

After standardization of the stimulated acid secretion parameters to the mean height of male plus female subjects, the sex differences disappear but male duodenal ulcer patients still were observed to secrete more than male controls (Table 3). Stimulated acid output in women with duodenal ulcer was not significantly different from that in control women, and the differences with regard to V_{obs} and V_g remain of borderline significance.

Pentagastrin- or histamine-stimulated acid output is the measurement reported in most studies. To assess the proportion of duodenal ulcer patients secreting more than the upper 95% confidence limit of secretion in controls, we counted the number of male patients secreting a maximal acid output greater than the mean plus 1.96 standard deviations in the male controls, which is 35.36 mmol/h; only nine patients were observed to secrete above this limit. Since the total number of male duodenal ulcer patients is 44, the proportion of duodenal ulcer patients secreting greater than the upper normal limit is 20.45%.

The gastric acid secretion parameters were compared between blood group O subjects and those in the other ABO groups among the control subjects and duodenal ulcer patients, each subdivided according to sex. Among the male control subjects, those in group O were found to secrete less basal V_{obs}, while group O female patients with duodenal ulcer were younger and secreted higher basal and stimulated V_g than did female patients belonging to other groups.

Duodenal ulcer patients were divided according to the presence or absence of a family history of peptic ulcer (Table 4). Male patients with a family history were noted to show significantly more stimulated acid output and V_{obs}, and suggestively more basal V_g, than did patients without a family history of the disease. Female patients with a family history of peptic ulcer tended to be younger than those with no family history but this difference was of borderline significance.

The effect of chronic cigarette smoking in male controls is shown in Table 5. Among the male controls, smokers were younger and showed significantly more stimulated acid output than did nonsmokers; the increase in stimulated V_g is of borderline significance. After standardization for height, the differences in stimulated acid secretion were of the same order of significance (Table 6) and acid output and V_{obs} positively and significantly correlated with smoking factors (Table 7). In male patients with duodenal ulcer, smokers tended to be older with a longer duration of illness than were nonsmokers, but the difference in acid secretion between smoking and nonsmoking patients was not significant. The situation was not altered by height standardization.

TABLE 2. *Summary of gastric acid secretion data in control subjects and patients with duodenal ulcers.*

Acid output		Control		Duodenal Ulcer	
		Male	Female	Male	Female
Basal					
Acid output (mmol/h)	N	25	11	44	14
	$\bar{X}$	1.78	1.76	3.81††	1.55[b]
	SD	1.49	2.02	3.42	2.37
V_{obs} (ml/h)	N	25	11	43	14
	$\bar{X}$	63.22	38.87[a]	69.11	49.73
	SD	37.96	24.27	44.22	37.11
V_g (ml/h)	N	24	9	39	14
	$\bar{X}$	99.58	71.34	134.96*	109.49*
	SD	68.20	38.82	71.00	46.82
Stimulated					
Acid output (mmol/h)	N	25	11	44	14
	$\bar{X}$	19.86	16.23[a]	27.08††	18.60[c]
	SD	7.91	4.33	9.54	7.53
V_{obs} (ml/h)	N	25	11	44	14
	$\bar{X}$	201.30	153.29[b]	240.98†	*200.95[a]
	SD	67.25	39.21	75.05	82.09
V_g (ml/h)	N	24	10	41	14
	$\bar{X}$	244.40	168.82[c]	259.31	231.94*
	SD	117.15	40.62	91.94	106.75

[a] for $0.1 > P > 0.05$; [b]for $P < 0.05$; and [c]for $P < 0.01$ when comparing between the sexes within either the control or duodenal ulcer group by Student's *t* test.

* for $0.1 > P > 0.05$; †for $P < 0.05$; and †† for $P < 0.01$ when comparing between control and duodenal ulcer patients within the same sex by Student's *t* test.

V_{obs} = observed volume; Vg = volume corrected for pyloric losses and duodenogastric reflux.

TABLE 3. *Maximal stimulated gastric acid secretion variables in control subjects and patients with duodenal ulcer after height standardization.*

		Control		Duodenal Ulcer	
		Male	Female	Male	Female
Acid output (mmol/h)	N	25	11	44	14
	$\bar{X}$	18.30	19.19	25.46††	21.72
	SD	7.15	5.74	9.01	8.88
V_{obs} (ml/h)	N	25	11	44	14
	$\bar{X}$	184.94	182.52	226.54†	233.06*
	SD	59.69	46.15	73.15	79.30
V_g (ml/h)	N	24	10	41	14
	$\bar{X}$	223.91	204.36	244.22*	272.95*
	SD	104.54	55.76	88.43	125.32

* For $0.1 > P > 0.05$; †for $P = 0.0182$; and †† for $P = 0.0011$, when comparing between duodenal ulcer and control groups for the same sex by Student's *t* test.

V_{obs} = observed volume; Vg = volume corrected for pyloric losses and duodenogastric reflux.

TABLE 4. *Effect of family history of peptic ulcer on patients with duodenal ulcer.*

		Males		Females	
Variables		Family history	No family history	Family history	No family history
No. of patients		7	37	2	12.
Mean age at onset of symptoms (y) ± SD		28.79± 12.12	31.13± 11.49	18.50*± 6.36	37.33± 11.97
Mean weight (kg) ± SD		61.43± 9.16	61.03± 10.09	61.00 ± 28.28	62.58± 14.10
Mean height (cm) ± SD		167.71± 4.39	163.86± 6.03	156.50 ± 10.61	153.08± 4.36
Mean LBM (kg) ± SD		47.52± 4.01	46.35± 4.59	40.18 ± 12.80	39.22± 4.62
No. in blood group O		3	21	2	7
Basal					
Acid output (mmol/h)	N	7	37	2	7
	$\bar{X}$	2.58	4.05	0.00	1.81
	SD	3.52	3.40	0.00	2.47
V_{obs} (ml/h)	N	6	37	2	12
	$\bar{X}$	62.35	70.20	34.71	52.24
	SD	35.12	45.84	12.09	39.57
V_g (ml/h)	N	5	34	2	12
	$\bar{X}$	190.15*	126.85	136.86	104.93
	SD	92.61	65.09	41.83	47.67
Stimulated					
Acid output (mmol/h)	N	7	37	2	12
	$\bar{X}$	33.83†	25.80	22.77	17.91
	SD	6.54	9.54	0.78	7.96
V_{obs} (ml/h)	N	7	37	2	12
	$\bar{X}$	298.82†	230.03	321.33	180.89
	SD	59.62	73.23	152.35	54.55
V_g (ml/h)	N	7	34	2	12
	$\bar{X}$	315.97	247.64	286.53	222.84
	SD	131.25	79.33	86.93	110.22

* For $0.1 > P > 0.05$ and † for $P < 0.05$ when comparing duodenal ulcer patients with family history of peptic ulcer with those with no family history within the same sex by Student's *t* test.

LBM = lean body mass; V_{obs} = observed volume; V_g = volume corrected for pyloric losses and duodenogastric reflux.

TABLE 5. *Effect of chronic cigarette smoking on gastric acid secretion in male control subjects.*

Variables		Non-smokers	Smokers
No. of patients		17	6
Mean age (y) ± SD		34.53± 13.94	25.17*± 5.19
Mean weight (kg) ± SD		68.59± 15.25	61.67± 14.01
Mean height (cm) ± SD		165.59± 6.20	164.67± 3.78
Mean LBM (kg) ± SD		49.15± 6.06	46.57± 5.35
Basal			
Acid output (mmol/h)	N	17	6
	$\bar{X}$	1.71	2.16
	SD	1.56	1.39
V_{obs} (ml/h)	N	17	6
	$\bar{X}$	66.50	57.04
	SD	42.89	28.05
V_g (ml/h)	N	16	6
	$\bar{X}$	102.35	102.50
	SD	79.91	42.42
Stimulated			
Acid output (mmol/h)	N	17	6
	$\bar{X}$	18.16	26.57*
	SD	6.88	8.07
V_{obs} (ml/h)	N	17	6
	$\bar{X}$	193.25	244.99†
	SD	63.45	57.67
V_g (ml/h)	N	16	6
	$\bar{X}$	247.28	257.42
	SD	132.65	87.70

† For $P = 0.094$ and * for $P < 0.05$ when comparing smokers with nonsmokers by Student's *t* test.

LBM = lean body mass; V_{obs} = observed volume; V_g = volume corrected for pyloric losses and duodenogastric reflux.

TABLE 6. *Effect of chronic cigarette smoking on height-standardized maximal stimulated gastric acid secretion in male control subjects.*

		Non-smokers	Smokers
Acid output (mmol/h)	N	17	6
	$\bar{X}$	16.59	24.79*
	SD	6.23	6.71
V_{obs} (ml/h)	N	17	6
	$\bar{X}$	176.19	228.36†
	SD	55.53	47.26
V_g (ml/h)	N	16	6
	$\bar{X}$	224.83	239.56
	SD	118.46	77.04

† For $P = 0.0534$ and * for $P = 0.0128$ when comparing smokers with nonsmokers by Student's *t* test.

V_{obs} = observed volume; V_g = volume corrected for pyloric losses and duodenogastric reflux.

Discussion

Using an accurate method for determining gastric acid secretion, this study, probably the first done in Saudi subjects, gives the pattern of normal gastric acid secretion for a Saudi population. Male controls showed a mean basal gastric acid secretion of 1.78 ± 1.49 (SD) mmol/h and a mean pentagastrin-stimulated maximal acid output of 19.86 ± 7.91 (SD) mmol/h. The equivalent values for female controls were 1.76 ± 2.02 and 16.23 ± 4.33 mmol/h, respectively.

Generally women secreted less gastric acid than did men, and this reached statistical significance for V_{obs} and V_g in the control subjects and for acid output in the duodenal ulcer group. The control and duodenal ulcer groups were matched with regard to age, weight, height, and LBM, but within each group, women were shorter and had lower LBM. Correlations of maximal gastric acid secretion parameters were strongest with height, and height standardization of these parameters in control subjects and patients with duodenal ulcer eliminated the differences in acid secretion between the two sexes in both groups. This argues in favor of the hypothesis that the sex difference in acid secretion is due to the difference in height, and confirms a similar result recently reported by Whitfield and Hobsley[6] for their control subjects.

Differences in gastric acid secretion between the duodenal ulcer patients and controls were significant among the males, but only of borderline significance for the females. Full significance would probably be achieved with a larger group of females. Male patients with duodenal ulcer secreted more acid than did the male controls during both the basal and stimulated periods. Only one fifth of the male patients with duodenal ulcer had a maximal acid output greater than the upper limit of the mean + 1.96 SD in the male control subjects. This pattern confirms the well-known overlap in the level of secretion between patients with duodenal ulcer and normal controls. Since height standardization did not alter the pattern of acid secretion or the level of significance between controls and patients with duodenal ulcer of the same sex, the increased acid secretion in duodenal ulcer disease cannot be attributed to a difference in height.

The increased frequency of blood group O

TABLE 7. *Correlation of height-standardized maximal gastric acid secretion parameters with smoking factors in male control subjects.*

y	=	a	+	bx		*r*	*P*
Acid output	=	17.8040	+	0.5951	SMF	0.5780	0.0039
Observed volume	=	190.0676	+	3.84133	SMF	0.4733	0.0225

SMF = smoking factor.

observed in our patients with duodenal ulcer (Table 1) tends to confirm the well-known association of blood group O with duodenal ulcer disease. In our series the association is significant for the duodenal ulcer female patients and it is in these patients that a younger age is combined with increased basal and stimulated V_g for those who are in group O. This points to the operation of genetic factors in duodenal ulcer disease, especially in females.

The significant association between a family history of peptic ulcer and the occurrence of duodenal ulcer in our series also confirms the presence of genetic factors in the etiology of duodenal ulceration. The results reported in Table 4 do not, however, firmly support the proposal of Lam[2] concerning two categories of patients with duodenal ulcer: those with an early onset of disease, acid hypersecretion, and strong family history of duodenal ulcers, and a late onset group with high prevalence of blood group O. The presence of an early onset group with positive family history is merely suggested by the results in the small number of female duodenal ulcer patients, while the association of family history with gastric acid hypersecretion occurs only among male duodenal ulcer patients. Group O distribution is not related to the presence or absence of family history of peptic ulceration. Definite conclusions in relation to all these factors can only be reached in a large series.

Smoking is an important environmental factor in Saudi Arabia, as indicated by our finding of an increased frequency of smokers among male patients with duodenal ulcer compared to male controls.

Most smokers preferred cigarettes to sheesha. The small number of sheesha smokers (two controls and one patient with duodenal ulcer) does not allow for meaningful comparison of gastric secretion between cigarette and sheesha smokers. Our conclusions therefore concentrate on the effects of cigarette smoking.

Duodenal ulcer smokers tend to be older and have a longer duration of symptoms than nonsmoking patients. This suggests that smoking is an environmental hazard that in time would result in duodenal ulcer disease in a certain proportion of individuals.

A number of workers[4-7] have reported that chronic smoking increases gastric acid secretion in patients with duodenal ulcer and in control subjects. We found that smoking increases gastric acid secretion in male control subjects and that after height standardization the effect is still present and acid secretion correlates positively with smoking factor. Smoking was not observed to increase gastric acid secretion in our series of male patients with duodenal ulcer. In view of the results in our control subjects, the lack of an effect of smoking in patients with duodenal ulcer was unexpected, especially since we earlier demonstrated an increase in stimulated V_g earlier in the study when the number of patients was smaller. One possible explanation for this discrepancy may be our considering ex-smokers as smokers. The acid secretion in some of our smokers who had stopped smoking over a long period might have regressed toward normal.

The mechanism by which chronic smoking leads to enhanced acid secretion is a matter of speculation.[7] Smoking for a long period may cause an increase in the parietal cell mass or may enhance the sensitivity of parietal cells to stimulation. Because smoking does not elevate serum gastrin concentration (unpublished observations, 1988), the effect may be mediated through increased vagal drive to the parietal cells, as suggested by the action of nicotine in rats,[12,13] but so far there is no direct evidence in humans that smoking leads to enhanced vagal stimulation.

Our studies of duodenal ulcer disease in the Saudi environment have thus confirmed the well-known feature of gastric acid hypersecretion in this condition. In addition we have demonstrated the contribution of genetic factors (increased frequency of blood group O and family history of peptic ulcer) and of smoking as a significant environmental hazard. Smoking seems to be etiologically important for men while genetic factors seem to predominate in women.

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PERINATAL MORTALITY AT THE ARMED FORCES HOSPITAL, RIYADH, SAUDI ARABIA: FIVE-YEAR REVIEW OF 22,203 BIRTHS

Abdul-Aziz Algwiser, Fachartz

أجريت دراسة عن حالات الوفاة إبان الولادة التي حدثت في مستشفى القوات المسلحة بين عامي ١٩٨٣م و ١٩٨٧م. وقد بلغ عدد الوفيات بسبب الشذوذات الولادية ١٠٤ حالات (بنسبة ٣٥,٦٪) من أصل ٢٩٢ حالة وفاة إبان الولادة. ومن بين الأطفال المئة وثمانية وثمانين الذين كانوا أسوياء التكوين ثم توفوا، توفي ٦٤ خلال الأسبوع الأول من الحياة، و ٢٥ أثناء الولادة، و ٩٩ قبل الولادة. بلغت نسبة الوفاة إبان الولادة ١٣,١ في كل ١٠٠٠ حالة ولادة، والإملاص ٦,٦ في كل ١٠٠٠ حالة ولادة، كما بلغت نسبة وفاة الوليد ٦,٦ كل ١٠٠٠ حالة ولادة حية. بالنسبة للأطفال أسوياء التكوين كان الوزن عند الولادة أقل من ١٥٠٠ غرام في ٢٢,٦٪ من حالات الإملاص وفي ٧٠,٣٪ في حالات الوفاة المبكرة للوليد. وفي حالات وفيات الوليد الأربع والستين كان ٧٠,٣٪ منها خلال الساعات الأربع والعشرين عقب الولادة. كما بقي على قيد الحياة ٢٣,٨٪ من الأطفال الذين تراوحت أوزانهم بين ٥٠٠ و ٧٤٩غ، و ٨٧,٩٪ من الذين تراوحت أوزانهم بين ٧٥٠ و ٩٩٩غ. أما المولودون بعملية قيصرية ووزنهم أقل من ١٠٠٠ غ فقد بقي ٧١,٤٪ منهم على قيد الحياة بالمقارنة مع ٤٦,٧٪ الذين ولدوا عن طريق المهبل. إن تحسين وسائل الإشراف والمراقبة أثناء الحمل، واكتشاف المضاعفات لدى الجنين والأم في مرحلة مبكرة، وتحسين مستوى العناية بالوليد سيؤدي إلى إنخفاض أكبر في نسبة الوفيات إبان الولادة.

A study was conducted of the perinatal deaths that occurred at the Armed Forces Hospital between 1983 and 1987. Congenital anomalies accounted for 104 (35.6%) of the 292 perinatal deaths. Of the 188 normally formed infants who died, 64 died within the first week of life, 25 died during labor, and 99 died ante partum. The perinatal mortality was 13.1 per 1,000 total births; stillbirth rate, 6.6 per 1,000 total births, and neonatal death rate, 6.6 per 1,000 live births. Among normally formed infants, birth weight was less than 1500 g in 22.6% of the stillbirth cases and in 70.3% of the cases of early neonatal death. Of the 64 neonatal deaths, 70.3% occurred within 24 hours of delivery. Survival occurred in 23.8% of those infants weighing 500 to 749 g and in 87.9% of those weighing 750 to 999 g. Those infants born by cesarean section who weighed less than 1000 g exhibited a 71.4% survival rate compared with 46.7% in infants born vaginally. Improved antenatal supervision and monitoring, early detection of fetal and maternal complications, and better neonatal care should help to further reduce perinatal mortality.

Perinatal mortality rates are important for identifying problems in obstetrical and early neonatal care. Large national perinatal mortality surveys conducted in Western countries have had a major influence in outlining problem areas and stimulating efforts toward reducing perinatal loss.[1-3] The definition of fetal death differs among various public health authorities, however, and this makes international comparison difficult.[4-15] Sociological and biological differences between countries and regions within countries further depreciate perinatal mortality figures as indicators of the adequacy of maternity services.[4,8,16-19] For the purpose of study, International Federation of Obstetrics and Gynaecology and the World

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Health Organization[20-24] recommended definitions were applied.

Several hospital-based perinatal mortality studies[25-32] have been conducted in Saudi Arabia. The first two reports,[32,33] also originating from the Riyadh Armed Forces Hospital, served as a basis for further examining perinatal mortality in the context of birth weight and mode of delivery. The information gained can then serve as the basis for outlining measures that will further reduce perinatal mortality.

Material and Methods

All babies born at the Riyadh Armed Forces Hospital between 1 January 1983 and 31 December 1987 comprised the study population. Data collected included birth weight, cause of death, time of death, mode of delivery, and the effect of mode of delivery on the survival of very-low-birth-weight infants. All newborns and stillborns weighing 500 g and over at or after 22 weeks of gestation were included in the study. Gestational ages were calculated from the menstrual history and sonographic assessment of fetal biparietal diameter, abdominal girth, thoracic diameter, and femoral length. Three infants weighing less than 500 g were excluded. Very low birth weight was defined as 1,500 g or less.

All perinatal deaths were reviewed monthly at a perinatal mortality meeting attended by both obstetricians and neonatologists. Because autopsy is not permitted in Saudi Arabia, cause of death was diagnosed from clinical observations. Causes of death were classified according to a modified version of the Aberdeen classification.[2,3,34] The causes of death were listed according to the fetal or maternal condition that was most likely to be directly involved in the fetal death. Prematurity was defined as gestation below 37 weeks whereas infants over 42 weeks were considered postmature. Preeclampsia was diagnosed when blood pressure rose to at least 140/90 mm Hg on more than one occasion after the 24th week of gestation in a patient with previously normal blood pressure.

Results

The total number of infants delivered at the Riyadh Armed Forces Hospital has increased from 3615 in 1983 to 5019 in 1987 (Table 1). After decreasing to 10.8 per thousand in 1985, the perinatal mortality rose to 13.1 per thousand in 1987. Of the 22,203 infants with a birth weight of 500 g and over, 147 were stillborn and 145 died within the first week of life, yielding a perinatal mortality of 13.1 per thousand total births, stillbirth rate of 6.6 per thousand total births, and neonatal death rate of 6.6 per thousand live births.

Table 2 shows the time of death in relation to birth weight in both normal and congenitally malformed infants. Birth weight in 38.8% of the normally formed infants who died was less than 1500 g. Of the 64 deaths among normally formed infants, 45 (70.3%) died in the first 24 hours of life. Multiple anomalies and neural tube defects accounted for the majority of congenital malformations in infants who died: 36.5% and 29.8%, respectively (Table 3). Table 4 shows the causes of death in relation to birth weight in normally formed infants.

Survival in normally formed newborn infants according to gestational age is given in Figure 1 and according to birth weight in Figure 2. Maternal disease was the predisposing factor in 14 (7.4%) deaths, all of which were stillbirths. Diabetes was present in ten, renal hypertension in one, essential hypertension in one, acute brucellosis occurring at 39 weeks' gestation in one, and a brain tumor in one.

TABLE 1. *Total number of patients, births, and perinatal mortality during the study period.*

	1983	1984	1985	1986	1987	Total
Total no. of mothers	3577	3952	4396	5069	4965	21,959
Total no. of infants	3615	4001	4440	5128	5019	22,203
Early neonatal deaths (%)	5.6	7.3	6.1	7	6.6	
Stillbirths (%)	10.5	6.5	4.7	5.7	6.57	
Perinatal mortality (%)	16.0	13.7	10.8	12.67	13.15	

TABLE 2. *Birth weights and times of death (in relation to labor) of normally formed infants and birth weights of infants dying from fetal abnormality.*

Time of death	Birth weight (g) 500–749	750–999	1000–1249	1250–1499	1500–1749	1750–1999	2000–2249	2250–2499	≥2500	Total
Antepartum	3	4	13	3	8	8	10	5	45	99
Intrapartum	1	1	1	2	–	–	5	1	14	25
Postpartum	16	12	10	7	4	2	3	3	7	64
Total	20	17	24	12	12	10	18	9	66	188
Fetal anomaly	1	11	10	8	9	4	10	11	40	104
Grand total	21	28	34	20	21	14	28	20	106	292

TABLE 3. *Site of anomaly.*

Site	No. (%)
Multiple	38(36.5%)
Central nervous system	31(29.8%)
Chromosomal	8(7.7%)
Heart	8(7.7%)
Lungs	3(2.9%)
Diaphragmatic hernia	5(4.8%)
Tracheoesophageal fistula	1(1.0%)
Bilateral polycystic kidneys	4(3.8%)
Musculoskeletal system	5(4.8%)
Conjoined twin	1(1.0%)
Total	104

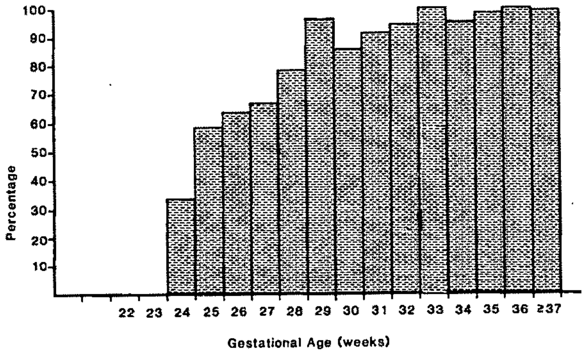

FIGURE 1. Survival in live born infants according to gestational age.

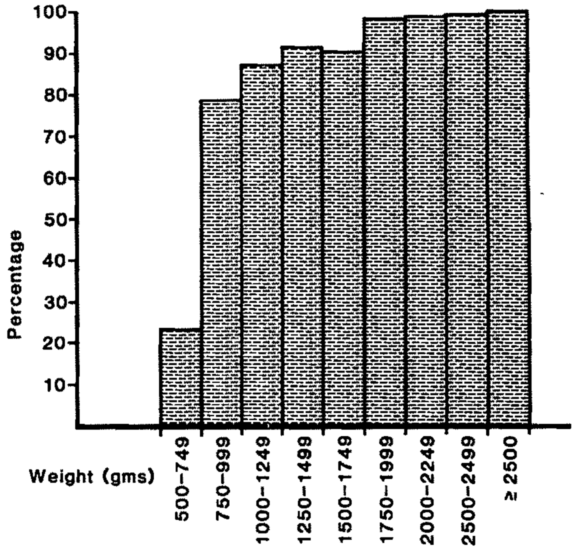

FIGURE 2. Survival of live born infants according to birth weight.

Mechanical factors accounted for 20 (10.6%) of the deaths among the normally formed infants: eight antepartum, ten intrapartum, and two neonatal. Thirteen babies weighed over 2500 g. The cord was tied around the neck in seven of the antepartum deaths and thrombosis of the umbilical cord was the cause of death in the eighth infant. Of the ten intrapartum deaths resulting from mechanical factors, four were related to difficult breech delivery, two to cord prolapse, and one to abruptio placentae following external cephalic version. The remaining three were due to difficult forceps delivery, two of which were associated with ruptured uterus. The two neonatal deaths were related to severe birth asphyxia, one an undiagnosed twin and one a difficult breech delivery through an incompletely dilated cervix.

Four deaths were due to severe rhesus isoimmunization, two of which were unbooked.

Eighteen deaths in normally formed infants were attributed to antepartum hemorrhage and this was due to abruptio placentae in eight cases, placenta previa in three cases, and an unknown site of bleeding in seven cases. Severe hypoxia was the cause of the eight neonatal deaths, two of which were associated with hyaline membrane disease and one with intraventricular hemorrhage. The ten intrapartum deaths were related to intrapartum asphyxia. Preeclampsia caused ten deaths: five stillbirths, two intrapartum deaths (both of which were complicated by abruptio placentae), and three neonatal deaths (one of which was complicated by abruptio placentae).

There were no maternal complications in 122 perinatal deaths occurring in normally formed infants (Table 4). Eight-five infants weighed less than 2500 g and 37 weighed over 2500 g. Of the 85 very-low-birth-weight and low-birth-weight infants who died, there were 43 neonatal deaths, two intrapartum deaths, and 40 stillbirths. Of the total 122, 71 were preterm, 17 of whom were severely growth retarded. Of 14 mature infants, ten were severely growth retarded. The causes of the 43 neonatal deaths in very-low-birth-weight and low-birth-weight infants were intrauterine hypoxia in two cases, respiratory distress syndrome in 22 cases, intraventricular hemorrhage in three cases, intraventricular hemorrhage associated with respiratory distress syndrome in six cases, infection in six cases, nonhemolytic

TABLE 4. *Causes of death in relation to birth weight and labor in normally formed infants.*

Birth weight (g) and time of death	APH	Pre-eclampsia	Maternal disease	Hemolytic disease	Mechanical problems	No maternal cause			Total
						VLBW	LBW	NBW	
500–749									
Pre PD	1	–	–	–	–	2	–	–	3
IPD	–	–	–	–	1	–	–	–	1
PPD	3	–	–	–	–	13	–	–	16
750–999									
Pre PD	1	–	–	–	1	2	–	–	4
IPD	1	–	–	–	–	–	–	–	1
PPD	2	1	–	–	–	9	–	–	12
1000–1249									
Pre PD	–	1	2	1	–	9	–	–	13
IPD	1	–	–	–	–	–	–	–	1
PPD	2	1	–	1	–	6	–	–	10
1250–1499									
Pre PD	–	–	–	–	–	3	–	–	3
IPD	–	1	–	–	1	–	–	–	2
PPD	–	1	–	–	–	6	–	–	7
1500–1749									
Pre PD	–	–	1	–	–	–	7	–	8
IPD	–	–	–	–	–	–	–	–	–
PPD	1	–	–	–	1	–	2	–	4
1750–1999									
Pre PD	–	1	–	–	–	–	7	–	8
IPD	–	–	–	–	–	–	–	–	–
PPD	–	–	–	–	–	–	2	–	2
2000–2249									
Pre PD	–	1	2	1	–	–	6	–	10
IPD	–	1	–	–	3	–	–	–	4
PPD	–	–	–	1	–	–	2	–	3
2250–2499									
Pre PD	–	–	–	–	–	–	5	–	5
IPD	1	–	–	–	–	–	1	–	2
PPD	–	–	–	–	–	–	3	–	3
≥2500									
Pre PD	1	2	9	–	8	–	–	25	45
IPD	4	–	–	–	4	–	–	6	14
PPD	–	–	–	–	1	–	–	6	7
Total	18	10	14	4	20	50	35	37	188

Pre PD = prepartum death; IPD = intrapartum death; PPD = postpartum death; APH = antepartum hemorrhage; VLBW = very low birth weight; LBW = low birth weight; NBW = normal birth weight.

hydrops fetalis in one, cot death in two, and intractable metabolic acidosis in one. Two infants died of severe birth hypoxia intrapartum and could not be saved by cesarean section.

Very-low-birth-weight infants (500 to 1499 g) constituted a large proportion of neonatal deaths in normally formed infants (70.3%). During the period of study there were 239 very-low-birth-weight infants; 45 died within the first week of life, giving a mortality rate of 188.3 per thousand live births among this group (Tables 5 and 6). The relationship of mode of delivery to survival in very-low-birth-weight infants is illustrated in Table 5 and this is further broken down by gestational age in Table 6. Table 7 shows the cause of death and Table 8 the Apgar scores at 1 and 5 minutes by weight and mode of delivery in very-low-birth-weight infants.

The causes of the 40 stillbirths were second twin in five cases, nonhemolytic hydrops fetalis in one case, and severe prematurity in 23 cases (of which 11 were severely growth retarded); the remaining 11 babies were full term but small for gestational age (eight were severely growth retarded).

Of the 37 perinatal deaths in infants weighing over 2500 g, six were neonatal, six occurred intrapartum, and 25 occurred before onset of delivery. The causes of the six neonatal deaths were birth asphyxia in three cases and one each of septicemia, recurrent convulsions, and cot death. The six intrapartum deaths were related to intrapartum asphyxia. Cesarean section was carried

TABLE 5. *Effect of birth weight and mode of delivery on survival of very-low-birth-weight infants.*

Birth	Vertex delivery			Breech delivery			Cesarean section		
weight (g)	No.	Survival	%	No.	Survival	%	No.	Survival	%
500–749	11	3	27.3	6	0	0	4	2	50
750–999	22	17	77.3	21	16	76.2	14	12	85.7
1000–1249	37	33	89.2	11	8	72.7	22	20	90.9
1250–1499	51	45	88.2	7	6	85.7	33	32	97.0
Total	121	98	81.0*	45	30	66.7*	73	66	90.4*

*Mean percentage.

TABLE 6. *Effect of gestational age and mode of delivery on survival of very low birth weight infants.*

Gestational	Vertex delivery			Breech delivery			Cesarean section		
age (wk)	No.	Survival	%	No.	Survival	%	No.	Survival	%
22	2	0	0	–	–	–	–	–	–
23	1	0	0	–	–	–	–	–	–
24	5	2	40	1	0	0	–	–	–
25	7	5	71.4	7	3	43.0	3	2	66.7
26	8	4	50.0	5	4	80.0	4	3	75.0
27	14	9	64.3	8	5	62.5	8	6	75.0
28	16	13	81.3	10	8	80.0	5	5	100.0
29	9	9	100.0	3	2	66.7	6	6	100.0
30	15	13	86.7	6	4	66.7	11	11	100.0
31	12	11	91.7	1	0	0	12	10	83.3
32	9	9	100.0	1	1	0	13	13	100.0
33	9	9	100.0	–	–	–	2	2	100.0
34	3	3	100.0	–	–	–	4	3	75.0
35	7	7	100.0	1	1	100.0	–	–	–
36	3	3	100.0	–	–	–	–	–	–
37	2	2	100.0	1	1	100.0	5	5	100.0
Total	122	99	81.1	44	29	65.9	73	66	90.4

TABLE 7. *Causes of early neonatal death of very-low-birth-weight infants by mode of delivery.*

Cause of death	Vertex delivery	Breech delivery	Cesarean section	Total
Prematurity	11	7	–	18
Intraventricular hemorrhage and respiratory distress syndrome	8	5	–	13
Antepartum hemorrhage	1	2	4	7
Preeclampsia	–	–	3	3
Infection	2	1	–	3
Hemolytic hydrops fetalis	1	–	–	1
Total	23	15	7	45

TABLE 8. *Mean Apgar score at one and five minutes in very-low-birth-weight infants.*

Birth weight (g)	Vertex delivery		Breech delivery		Cesarean section	
	Alive	Died	Alive	Died	Alive	Died
500–749	5 – 7	2 – 1	–	3 – 2	4 – 6	2 – 2
750–999	5 – 8	4 – 4	4 – 8	1 – 2	6 – 9	2 – 2
1000–1249	7 – 8	4 – 4	5 – 7	3 – 4	7 – 8	4 – 3
1250–1499	7 – 9	5 – 6	5 – 7	7 – 9	5 – 8	4 – 3

out in four cases but failed to save the baby. The causes of the 25 antepartum deaths were nonhemolytic hydrops fetalis in two cases, postmaturity in three, and undetermined cause in the remaining 20 cases.

Discussion

The most frequent cause of perinatal mortality in the present study was fetal abnormality, which accounted for 35.6% of the deaths. The incidence of fatal congenital anomalies was 4.7 per 1,000 total births. This rate is higher than that reported by others[3,11,15,16,26,35] but similar to that reported in Scotland for Avon and the Mersey region.[2,36,37] The high rate in the present study may be explained by the high incidence of consanguineous marriages among Saudis. Of the patients attending antenatal clinics of the Armed Forces Hospital, 25% were married to their first cousin.

Of normally formed infants, 52.7% died before the onset of labor, which agrees with the figures reported by Buckell[3] (49%) and McIlwaine[2] (41%). Of normally formed newborn infants, 70.3% died during the first 24 hours of life. Buckell[3] reported 52% and Mutch[36] 57%.

Almost half of the neonatal deaths in the present study were due to extreme prematurity. Despite the progress made in introducing pharmacological agents to stop premature labor, their overall impact in reducing the number of births before 28 weeks of gestation has been disappointing. Infants weighing less than 1500 g accounted for 38.3% of the deaths in normally formed infants. The neonatal mortality rate in this group was 188.3 per 1000 live births. This is similar to the figures cited by others.[38-42] Survival is closely related to birth weight. Babies weighing 500 to 1499 g have an 89.5% chance of being born alive and 81.2% chance of surviving the neonatal period. Those babies weighing 1000 to 1499 g have an 89.4% chance of survival as compared to a 64.1% chance of survival in babies weighing 500 to 999 g.

Mode of delivery seems to play a role in the survival of very small babies. Cesarean section seems to improve the chance of survival.[41] This was seen in the present study for those infants with birth weight of 500 to 999 g, but no significant difference was demonstrated between vertex and cesarean delivery for infants with a birth weight of 1,000 to 1,499 g. Cesarean section has been advised for breech presentation babies with a potential birth weight of under 1500 g.[38,40,43,49] Although the present report includes a relatively small number of infants in this birth weight range, compared to numbers considered in other studies,[42,47,50,51] there was significantly decreased survival in infants with breech presentation delivered vaginally for the 500 to 749 g and 750 to 999 g birth weight groups. An attempt to relate survival to mode of delivery or presentation of very-low-birth-weight infants may be statistically valid but may not be clinically applicable because of the need for cesarean section. Those infants with a low 5-minute Apgar score suffered intrapartum asphyxia. Thus perinatal asphyxia may have precipitated the subsequent development or increasing severity of respiratory distress syndrome[52] and intraventricular hemorrhage,[53] both factors shown to significantly increase mortality. The high proportion of neonatal deaths seen during the first 24 hours of life in the present study, and observed in other studies as well,[3,36] reinforces the need for expert care during that vital time. However, many more infants are lost before onset of labor. If perinatal mortality is to be reduced further, priority must be given to the following items:

1. Antenatal care must be improved in order to decrease the impact of maternal diseases such as diabetes, preeclampsia, and abruptio placentae, leading to a possible decrease in the number of unexplained fetal deaths.
2. More effective means must be devised to stop or delay premature labor, especially prior to 30 weeks' gestation.
3. The management of very-low-birth-weight infants must be improved through the implementation of better pediatric services.
4. Perinatal infections must be more effectively diagnosed and treated.
5. Further consideration and study must be devoted to the appropriate mode of delivery of small infants.

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EPIDEMIOLOGY OF ACCIDENTAL POISONING OF CHILDREN IN RIYADH, SAUDI ARABIA

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أجريت دراسة لتحديد مدى وقوع حالات التسمم العارض عند الأطفال ممن أدخلوا بسبب التسمم إلى المستشفيات الحكومية في الرياض خلال عام ١٩٨٨م. كانت العقاقير أكثر عوامل التسمم شيوعاً، إذ بلغت نسبتها ٥٢٪ من مجموع الحالات. كما بلغت نسبة التسمم بالكيروسين وابتلاع المنظفات المنزلية = ٤٦٪ من الحالات، فيما بلغت نسبة التسمم بابتلاع النباتات ٢٪ فقط. وحدثت معظم إصابات التسمم بين الأطفال الذين تتراوح أعمارهم من عام إلى عامين. تشير نتائجنا إلى أن تحسن الظروف المعيشية، والتخزين السليم للعقاقير والمواد الكيميائية، والتوعية الصحية للآباء والامهات ستساعد على الاقلال من وقوع حالات التسمم.

A study was carried out to determine the incidence of accidental poisoning in children admitted to Riyadh Governmental Hospitals during 1988. Drugs were the most common poisoning agent and accounted for 52% of all cases. Kerosene poisoning and ingestion of household cleansers accounted for 46% of the cases, and ingestion of plants represented 2% of cases. Most of the poisoning incidents occurred in children who were 1 to 2 years of age. Our findings indicate that improved living conditions, proper storage of drugs and chemicals, and health education of parents will help to reduce the incidence of poisoning.

Accidental poisoning represents a serious source of childhood morbidity and mortality throughout the world.[1-3] Various studies have shown a clear distinction in the pattern and extent of poisoning among children between developed and developing countries, and this reflects attitudinal and behavioral differences.[2-4]

There are few reports on the epidemiology of accidental poisoning in the Kingdom of Saudi Arabia.[4-6] Therefore, we conducted a prospective study to define the local pattern of childhood poisoning and to provide a basis for its prevention.

Material and Methods

The study was conducted from January through December 1988 on three days of a week in all children up to 12 years of age who were admitted to the following Riyadh hospitals: Children's Hospital, Armed Forces Hospital, King Khalid University Hospital, Security Forces Hospital, and National Guard Hospital. A special form was prepared to record the age and sex of the patient, type of poisoning, time of poisoning, source of poison, time before presentation at hospital, treatment, complication, final outcome, and duration of hospital stay.

Results

During the study period, there were 794 cases of poisoning in children and this constituted 4.9% of the total medical pediatric admissions. There was no seasonal variation in the incidence.

Table 1 shows the age and sex distribution of the children. Ages ranged between 3 months and 12 years, with a peak at one year. Most cases (92%) occurred in children younger than five years. There were 422 males and 372 females (ratio, 1.1:1.0), which did not achieve statistical significance ($P > 0.05$) when analyzed with respect to age.

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TABLE 1. *Age and sex distribution of accidental poisoning.*

Age (y)	Male	Female	Total
0–<1	49	43	92
1–<2	120	115	235
2–<3	106	110	216
3–<4	73	57	130
4–<5	34	26	60
5–<6	12	7	19
6–12	28	14	42
Total	422	372	794

TABLE 2. *Summary of cases according to type of poisoning.*

Poison agent	No.	%
Medicine		
Salicylate	80	10.1
Acetaminophen	74	9.3
Contraceptives	58	7.3
Iron	52	6.5
Barbiturates	33	4.2
Cough syrup	25	3.1
Antiemetic	22	2.8
Anticholinergic	7	1.0
Others	14	1.7
Unidentified drugs	50	6.3
Subtotal	415	52.3
Household products		
Kerosene	194	24.4
Chlorine bleach	102	12.8
Detergent	30	3.8
Insecticides and rodenticides	11	1.4
Others	28	3.5
Subtotal	365	46.0
Plants	14	1.7

Most affected children belonged to the family equivalent of social classes IV (semiskilled) and V (unskilled). In 78% of the cases the child's father had an elementary school education and the mother no formal education. Only 5% of the children lived in a villa: 42% lived in flats and 35% in small detached houses in the poor quarters of Riyadh. The remaining 18% lived in mud houses or tents.

Table 2 breaks down the cases according to the type of poisoning. Drugs were the most common source and accounted for 52% of all cases. This was followed by products (46%) and plants (2%).

The most common drugs ingested included analgesics and antipyretics (19.4%), contraceptives (7.3%), iron supplement syrup (6.5%), barbiturates (4.2%), cough syrup (3.1%), antiemetics (2.8%), and unidentified drugs (6.3%). Kerosene was the most common household agent ingested and accounted for 24.4% of all cases. Household chemicals (bleach and detergent) accounted for 16.7% of all cases, insecticide and rodenticide, 1.4%; and unidentified agents, 3.5%.

Clinical Features

Kerosene: It was impossible to quantify the amount of kerosene ingested and thus symptoms could not be related to the quantity consumed. Forty-one percent of the children affected exhibited no symptoms. In the remainder the most common clinical features were vomiting (41%), followed by fever (29%), diarrhea (22%), cough (17%), abdominal pain (15%), and unconsciousness (1%). Clinical signs of pneumonitis consisting of dyspnea, intercostal and subcostal recession, and crepitations existed in 71 (13%) cases. Radiological examination confirmed pneumonia in 34 (48%) cases.

Drugs: Of the children admitted with drug poisoning, 23% were asymptomatic, 64% presented with vomiting, and 33% were in varying degrees of unconsciousness. Metabolic acidosis was verified by laboratory studies in 13% of the cases.

Other poisons: In the remaining children who were poisoned by other agents, the presenting features included vomiting, diarrhea with dehydration, abdominal pain, and restlessness.

Management

First aid was administered at home in 32% of the children and this was done mainly in children who had ingested kerosene. No treatment was given in the remaining 68%.

The majority of the patients (61%) were seen four hours after the poisoning episode; only 6% were seen within 2 hours. Gastric lavage was carried out in 33% of the patients (all cases of non-kerosene poisoning). In the cases of kerosene poisoning, patients with clinical evidence of pneumonitis were treated with antibiotics.

Forty-two percent of the patients were discharged within 24 hours of admission and only 12% stayed beyond 96 hours. Mean hospitalization time was 48 hours.

Discussion

This study shows that accidental poisoning is a major health problem in Saudi Arabia. Of the total annual medical admissions to the main pediatric department, 4.9% were cases of poisoning. This rate is higher than those reported for other developing countries,[8-10] but lower than those for Britain and the United States.[11-14]

As with other published studies,[5-8,10,11] we found no significant difference in the distribution of cases by sex. We found a high incidence of accidental poisoning in children between 1 and 5 years of age and this agrees with the rates cited in other reports.[4-6,8,10,11] This age is characterized by impulsive behavior, curiosity, thoughtlessness, and lack of experience. Few cases occurred in children younger than one year, probably because infants are more limited in their mobility, or after age five when children are more discriminating about what they swallow.

Unlike other developing countries where household products represent the most frequent cause of accidental poisoning, in Riyadh drugs constitute a greater problem.[8-10] One reason for this is that medications are dispensed in loose plastic envelopes rather than in child-resistant containers. In some hospitals, drugs are dispensed without appropriate labels giving the drug name, dosage, and date. Careless storage of drugs at home is another contributing factor. In the present study, 19% of the cases of drug poisoning were caused by analgesic or antipyretic consumption. These drugs are used commonly at home for the treatment of fever and pain.

Kerosene, which is used for cooking and heating in some parts of Riyadh, is the most common household agent causing poisoning and accounts for 54% of the accidents due to household products and 24% of the total number of cases. This percentage is less than those reported for developing countries,[9,10] but is still higher than those reported for developed countries.[11,12] Careless storage is responsible for most cases. The situation observed in Riyadh is similar to that seen elsewhere in Saudi Arabia.[4-7]

An in depth, prospective epidemiological study is needed that will identify the factors associated with accidental poisoning in Saudi Arabia. In this way effective preventive measures can be implemented. In the meantime, various effective preventive measures adopted in other countries can be used.[1,2,15,16]

Education of parents and other caregivers of young children will help reduce the morbidity and mortality associated with accidental poisoning. Educational pamphlets describing the hazards and safe storage of all potentially toxic substances at home are helpful aids. The widespread use of child-resistant containers is necessary to combat the number of drug-related poisonings. If it is not practical for all medications to be issued in such containers, then this should be done for a selected number of dangerous compounds. This has proved effective in developed countries.[12-15] A committee is needed to regulate the number of registered brands of medicines.

Regional poisoning control centers are an important step toward the rapid identification and treatment of poisoning accidents and are also important in their prevention through planning, research, and education.

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ACUTE DIARRHEAL DISEASE IN CHILDREN UNDER FIVE YEARS OF AGE IN THE EASTERN PROVINCE OF SAUDI ARABIA

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أجريت دراسة متابعة ل ٨٥٩ طفلاً تقل أعمارهم عن خمس سنوات سبقت معالجتهم من الإسهال الحاد في مركز مكافحة الإسهال، في الدمام، خلال عام ١٤٠٨هـ (١٩٨٧ ـ ١٩٨٨م). كان الهدف من الدراسة هو استقصاء المُمْرضات المعوية .المحتملة التي سببت الإسهال لدى هؤلاء الأطفال. ثم عزل مُمْرضات معوية من عينات البراز في نسبة ٥٢,٦٪ من الأطفال. تمت مشاهدة الخمج بجراثيم متعددة في نسبة ٠,٨٪ من الأطفال. من المُمْرضات المعوية التي تم عزلها وكانت الأكثر تواردًا بالترتيب التنازلي روتافايروس، السلمونيلة، الشيغلَة كامبيلوباكتر جيجوني، وتلي ذلك المرضات المعوية الاشريكية القولونية و الضمات غير المتراصة. رافق الخمج بالروتافايروس التهاب تنفسي وحمى في نسبة ٣٠٪ من الأطفال. وكان أكثر ما عزل من الطفيليات الجياردية اللمبلية.

A follow-up study was conducted in 859 children younger than 5 years who were treated for acute diarrhea at the Diarrhoea Control Center, Dammam, during 1408H (1987-1988). The purpose of the study was to investigate the potential enteropathogens responsible for causing diarrhea among these children. An enteropathogen was isolated from stool samples in 52.6% of the children. Multiple infections were seen in 0.8% of the children. The most common enteropathogens isolated, in descending frequency, were rotavirus, *Salmonella*, *Shigella*, and *Campylobacter jejuni*, followed by enteropathogenic *Escherichia coli* and nonagglutinating vibrios. Rotavirus infection was accompanied by respiratory infection and fever among 30% of the children. The most common parasite isolated was *Giardia lamblia*.

Five hundred million cases of acute diarrhea occur each year in children under 5 years of age throughout the world[1] and it imposes a heavy burden on health services. The disease occurs predominantly in the pediatric age group and is detrimental to the general health of children.

As the result of recent research findings, it is now possible to identify causative agents in some 70 to 80% of cases of diarrhea seen at treatment centers. New enteropathogens have also been identified, including rotavirus, *Campylobacter jejuni*, and *Escherichia coli* (enterotoxigenic and enteroinvasive).[2]

Since routine culture is not practical in most situations, simple diagnostic schemes are needed for use in areas with limited laboratory facilities to identify invasive types of diarrhea. Antibiotics are primarily of value in cholera and dysentery, and antiparasitic agents are useful for symptomatic infections with *Giardia lamblia* and *Entamoeba histolytica*.[3]

The present study of acute diarrhea in children under 5 years of age was conducted at the Diarrhoea Control Center, Dammam, during 1987-88 with the main objective to investigate common bacterial and viral agents causing diarrhea and to determine clinical features relevant to the diagnosis of the illness.

Material and Methods

The study population consisted of all children below 5 years of age who came to the Diarrhoea

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Control Center, Dammam, with a history of acute diarrhea of not more than 72 hours' duration. Diarrhea was defined as the passage of three or more stools per day with change in the consistency. The main criteria for inclusion in the study were: an untreated child who did not receive any antibiotics during the episode and from whom a fresh stool sample was collected. A standard protocol was used for recording the history and findings of the clinical examination. Fresh stool samples were examined for the presence of blood and mucus. Microscopic examination was carried out for the presence of fecal leukocytes and erythrocytes, and for parasites and their ova cysts using a standard technique.[4] Direct plating of the stool sample was done to detect enteropathogens, and enzyme-linked immunosorbent assay was used to detect rotavirus in the stool samples from children below 2 years of age using the technique of Rubenstein et al.[5] The chi-square test, *t* test, and analysis of variance were applied for statistical analysis.

Results

A total of 859 children of both sexes were studied. All were younger than 5 years old and all had acute diarrhea. They comprised 24% of such children attending the Diarrhoea Control Center during the study year. Children under 1 year of age represented 43.4% of the total and children over 1 year of age, 56.6%.

Most of the children presented with mild to moderate dehydration and they represented all age groups. Moderate dehydration constituted only 15% of the total. Only 1.6% of the children with acute diarrhea were treated with intravenous rehydration because of profuse vomiting. This was later followed by oral rehydration therapy.

The invasive type of diarrhea was seen in 33.6% of the children, as shown by the presence of fecal leukocytes or red blood cells, or both, in the stool sample. Parasites were isolated among 8.7% of the children. *Giardia lamblia* formed the bulk of such cases (6.8%) and *Entamoeba histolytica*, 0.3%.

Table 1 is a summary of the enteropathogens isolated during stool culture. An enteropathogen was isolated from 52.6% of the children, and 0.8% of the children had multiple infection. Rotavirus was isolated from 37.5% of the children under 2 years of age.

TABLE 1. *Isolation of enteropathogens in children younger than 5 years.*

	No.	Percentage
Organism		
Rotavirus	240 (< 2 yr)	37.5
Salmonella	60	7.0
Shigella	40	4.7
Campylobacter jejuni	14	1.6
Enteropathogenic *Escherichia*	8	0.9
Nonagglutinating vibrios	8	0.9
Mixed	7	0.8
No. of organisms		
One	452	52.6
Nil	400	46.6
Multiple	7	0.8

Age-specific isolation rates are shown in Table 2. Rotavirus was detected in 39.4% of the children below 1 year of age and in 34.8% of those between 1 and 2 years. *Salmonella* was isolated in 9.4% of the children below 1 year of age. The regression coefficients of age were found to be not significant.

Clinical features of the diarrhea in 70% of the children with *Shigella* infection consisted of abdominal pain and blood and mucus in the stools, and this showed significance at $P < 0.001$ (Table 3). Watery diarrhea was observed in 60% of the children with rotavirus infection, and this showed significance at $P < 0.001$. Diarrhea and vomiting occurred in 38% of the children and fever in 30%. Fever was observed in 50% of the children with *Salmonella* infection.

Discussion

Most of the infants and children in our study were below 3 years of age, representing 83.7% of the total study group who presented with acute diarrhea along with mild to moderate dehydration. No severe dehydration was found in any child, and this could be due to good nutritional status or early institution of oral rehydration therapy in these children. Microscopical analysis of stool samples was highly useful in differentiating invasive from noninvasive forms of diarrhea. It detected leukocytes and/or red blood cells in

TABLE 2. *Age-specific isolation rates of different enteropathogens.*

Age	No.	Rotavirus	*Salmonella*	*Shigella*	*Campylobacter jejuni*	EPEC	Others
<1 yr	373	147 (39.4)	35 (9.4)	5 (1.3)	5 (1.3)	4 (1.1)	11 (2.9)
1–2 yr	267	93 (34.8)	12 (4.5)	8 (2.9)	–	–	–
2–3 yr	79	–	5 (6.3)	9 (11.4)	4 (5.0)	3 (3.8)	8 (10.1)
3–5 yr	140	–	8 (5.7)	17 (12.1)	5 (3.6)	1 (0.7)	1 (0.7)
Total	859	240 (27.5)	60 (7.0)	40 (4.7)	14 (1.6)	8 (0.9)	20 (2.3)

Analysis of variance table

Source of variation	Sum of square	Degree of freedom	Mean square	Completed f.
Regression	4117.74	3	1372.58	0.99
Error	20597.22	15	1373.25	
Total	24714.96	18		

F > F [0.95; 3,15] = 3.29; f = 0.99.
EPEC = enteropathogenic *Escherichia coli.*

TABLE 3. *Signs, symptoms, and etiology of patients below 5 years.*

	Rotavirus	*Salmonella*	*Shigella*	*Campylobacter jejuni*
	N = 240	N = 60	N = 40	N = 14
No. of stools/day	7.3 ± 4.7* ($P<0.01$)	3.5 ± 1.02	6.5 ± 0.68	5.5 ± 0.23
Watery diarrhea	148† (61.7) ($P<0.001$)	18 (30.0)	–	–
Watery diarrhea and vomiting	92 (38.3)	18 (30.0)	12 (30.0)	2 (14.3)
Abdominal pain	48 (20.0)	18 (30.0)	4 (10.0)	10 (71.4)
Fever	72† (30.0) ($P<0.001$)	30 (50.0)	8 (20.0)	1 (7.1)
Abdominal pain with blood/mucus	–	24 (40.0)	28† (70.0) ($P<0.001$)	2 (14.3)
Upper respiratory tract infection	72† (30.0) ($P<0.001$)	18 (30.0)	12 (30.0)	–

Significance of the difference between marked etiology and other etiology.
**t* test, $P<0.01$; †chi-square test, $P<0.001$.

33.6% of the stool samples. *Giardia lamblia* was the most prevalent parasite and was found across all age groups in 6.8% of the children. *Entamoeba histolytica* was present in only 0.3% of the children older than 3 years. Children who were entirely breast fed exhibited no parasites in their stools. The invasive type of diarrhea was more common in older children.

The enteropathogens isolated in 53.4% of the children in our study represent a broad range of pathogens responsible for causing diarrhea and our findings agree with those reported elsewhere.[6-9] If we had investigated for enterotoxogenic *Escherichia coli*, this percentage could have been higher. Rotavirus, isolated in 37.5% of the children, was the most important cause of diarrhea, particularly in children younger than 2 years. This finding does not differ from those reported from other countries.[10-13] Rotavirus is recognized as a leading cause of gastroenteritis in newborn nurseries and the existence of an asymptomatic infection cannot be ruled out. A recent study[14] cited a 12% incidence of asymptomatic infection, though some studies have shown higher figures.[15]

Common enteropathogens, after rotavirus, were *Salmonella, Shigella, Campylobacter*, enteropathogenic *Escherichia coli*, and nonagglutinating vibrios, in order of frequency. *Salmonella* was found in 9.4% of children under 1 year of age, and there was an increase in *Shigella* and *Campylobacter* infection with increasing age. Higher rates have been reported by others,[16-18] and this could be due to varying regional characteristics or seasonal differences. In our study, we found that rotavirus infection was common during colder months (December to March) with a peak of 59% in early March. *Salmonella* infection increased to 20% during summer months. *Shigella* infection did not show any variation but was prevalent throughout the year.

There was considerable overlap in the clinical findings among patients with acute diarrhea and these were helpful in diagnosing only rotavirus and *Shigella* infections. Vomiting and/or watery diarrhea were the initial symptoms in rotavirus infections. Upper respiratory infection was seen in 30% of the children with rotavirus infection, and this was accompanied by a fever of more than 38°C. Other studies have revealed similar findings.[19] *Shigella* infection predominantly presented with a dysentery-like syndrome but no child presented with watery diarrhea. A similar correlation of clinical features has been found in studies conducted in India and Bangladesh.[7,20] No distinct clinical features were apparent for enteropathogenic *Escherichia coli* and *Campylobacter jejuni* infections.

Isolation of the enteropathogens indicates a wide range of microorganisms responsible for the infections. Only about 20% of the cases of acute diarrhea in the pediatric age group studied are caused by enteropathogens. Routine treatment for these infections consisted of antibiotics along with oral rehydration; otherwise all children were treated by oral rehydration therapy only.

Community studies are essential because the data derived can be useful for defining the etiological pattern and antibiotic sensitivity and this knowledge applied in the treatment of local cases. Precise etiological diagnosis is not essential for the immediate care of the diarrhea patient, as oral rehydration is the primary treatment in all cases of diarrhea regardless of patient age and cause.[21] Clinical presentation and stool examination of the diarrhea patients can be useful in starting the presumptive treatment.

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RETROSPECTIVE APPRAISAL OF 300 CONSECUTIVE MAMMOGRAMS

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تمت مراجعة ثلاثمائة صورة شعاعية متتالية للثدي بناء على قرائن انتقاء معينة مع مراجعة بيانات سريرية وإمراضية ذات علاقة بها. كان العمر الوسطي ± الإنحراف المعياري للنساء المؤهلات ٣٦,١١ (± ١١,٢ سنة). بلغت نسبة السيدات السعوديات ٦٥٪ (١٩٦ سيدة) من مجموعة الدراسة، وغير السعوديات ٣٥٪ (١٠٤ سيدات). كانت نتائج ٧٣ سيدة (٢٤٪) طبيعية، ولكن ظهرت إصابة ١٧٧ (٥٩٪) بالمرض الكيسي الليفي، و ٢٦ (٩٪) بسرطان غاز (متغلغل)، و ٢٤ (٨٪) بغدوم ليفي. تم طلب ٩٩ بالمئة من هذه الصور الشعاعية لسيدات كن يعانين من أعراض ثديية لعدة شهور. وكانت مريضات السرطان على علم بوجود الكتلة في الثدي لديهن لفترة وسطية طولها ٨,٠٤ (± ٢,١١ ا ع) شهرًا. كانت جميع الحالات السرطانية غازيَة (متغلغلة) وكان معظمها (٩٢,٣٪) في مرحلة متقدمة وقت التشخيص. من بين حالات المرضى الكيسي الليفي البالغ عددها ١٧٧، تبين أن ستًا (٣٪) منهن فقط يعانين من فرط التنسج اللانمطي، إلا أن نسبة انتشاره أقل مما نشر مؤخرًا. كان التوافق بين التشخيص النهائي وتشخيص الصور الشعاعية للثدي ذا أهمية احصائية (P-0.027). كما أظهرت النتائج ارتفاع نسب نوعية (٧٩٪)، وحساسية (١٠٠٪)، ودقة (٨٩٪) التصوير الشعاعي للثدي في مريضات السرطان، حيث أن قدرة التصوير الشعاعي للثدي على إظهار الخباثة قد تأكد بواسطة التحليل التراجعي المتعدد. إن بياناتنا المأخوذة من عينة من النساء اللواتي تمت معاينتهن في أحد مراكز التخصصية (الثالثية) قد ألقت بعض الضوء على نمط آفات الثدي في جمهرة مرضانا، ويجب الافادة من هذه البيانات في مجال التخطيط لإنشاء برنامج وطني للكشف المبكر عن سرطان الثدي.

Based on certain selection criteria, 300 consecutive mammograms were reviewed, together with other relevant clinical and pathological data. The median age (± SD) of eligible women was 36.11 (± 11.2 years). Saudis represented 65% (196 women) of the study population and non-Saudis 35% (104 women). Seventy-three women (24%) had normal findings but fibrocystic disease was found in 177 (59%), invasive carcinoma in 26 (9%), and fibroadenoma in 24 (8%). Ninety-nine percent of the mammograms were ordered in women who had had breast symptoms for several months. Cancer patients had been aware of their breast lump for a mean of 8.04 ± 2.11 (SD) months. All cancers were invasive and most (92.3%) were advanced at diagnosis. Among the 177 patients with fibrocystic disease, only six (3%) were found to have atypical hyperplasia, but its prevalence is lower than that reported recently. Agreement between final and mammographic diagnoses was significant ($P = 0.027$). Also shown were the high specificity (79%), sensitivity (100%), and accuracy (89%) of mammograms in cancer patients. The ability of mammography to show malignancy was proven by multiple regression analysis. Our data taken from a sample of women seen at a tertiary care facility shed some light on the pattern of breast disorders in our patient population. The data should be utilized in the planning for a national breast cancer early detection program.

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Radiographic examination of the breast is not a new procedure. The first mammographic study was made by Salomon in 1913 and the first clinical paper on the subject was published in 1930 by Warren.[1] Since then, mammography has proved its value in the diagnosis of various breast diseases. However, it was not until 1956 that the procedure was introduced for the mass screening of healthy women in the early detection of breast cancer.[2] Analysis of data derived from these major screening projects has shown an unequivocal benefit for women older than 50 years of age.[3-5]

In Saudi Arabia, several retrospective observational studies[6,7] and a recent review[8] have shown that breast cancer is the most common cancer type in Saudi females, constituting about 17% of all malignancies. Despite its high prevalence, the attitude of local physicians and that of asymptomatic females toward screening mammography has not been assessed. Conversely, there are no data about the prevalence of benign breast disorders among Saudi females. We therefore studied the pattern and prevalence of various breast disorders found in patients seen at a tertiary care facility, based on mammographic findings. The correlation between radiological or clinical data and final diagnosis was also examined. The attitude toward screening mammography could only be assessed indirectly by reviewing the various indications for ordering mammography.

Material and Methods

Film mammography was introduced to our hospital in 1983. The radiology log book was reviewed for the period 1983 to 1988, and all mammographic studies done as follow-up on patients with known breast cancer were excluded. Also excluded were those mammograms that were not supported by histological confirmation. However, mammograms were included for those patients in whom biopsy was not done but whose subsequent clinical course pointed to a specific diagnosis or confirmed the normal mammograph findings. Patients referred from other hospitals for mammography only and not for further care were excluded if complete clinical or follow-up data were not available. Only the first mammogram performed for each of the first consecutive 300 eligible patients was included in the analysis. All evaluable studies were done and interpreted by the same senior radiologist (A.Y.E.) and further assessed by a senior radiology resident (F.A.A.). The medical records of all eligible patients were retrieved and all relevant data were captured.

Prior to each mammogram, complete patient history was obtained and clinical examination of both breasts was done by the radiologists. During mammography, compression was applied and craniocaudal and mediolateral views were taken for each breast using a Siemens Mammomat B (automatic/manual) at 16-800 milliampere/second (MAS) at 28 to 30 kV with an automatic setting for the MAS. MR3 film (Agfa mammoray, single emulsion) and a fast screen were used.

Because of the retrospective nature of the study, the initial radiologist was not blinded to the indication for ordering mammogram or the clinicians' findings. However, for the purpose of the current analysis, all studies were reviewed without knowledge of the diagnosis and the findings that were initially reported. Radiologists were also blinded from the patients' subsequent course and any repeated mammograms.

Diagnosis of various mammographic patterns was based on the mammographic description of the general texture of the breast tissue. To accurately interpret a mammogram, structural detail must be visualized throughout the breast and also there must be sufficient resolution. The presence of any mass was further assessed for its size, site, consistency, and configuration. The presence or absence of calcification, especially microcalcification, was particularly evaluated. Subcutaneous reaction, skin thickening, and nipple changes were also examined.

A computerized database was constructed in which all study data were entered as coded variables or actual values using a database program and a personal computer. Use of the unique medical record number assigned to each patient avoided the potential error of double entry. Final diagnosis was defined as the diagnosis that was confirmed histologically or proven clinically by the subsequent follow-up course. The specificity of mammography is considered as the probability of a true-negative being detected as negative by the procedure; it is one minus the false-positive rate. The sensitivity of the mammography is considered as the probability of a true-positive being detected as positive by the procedure; it is one minus the false-negative rate. The accuracy is the percentage of all mammographic procedures that correctly predict the result, either positive or negative. Comparison between proportions was tested for significance using chi square or Fisher's exact test when appropriate.[9] Testing the difference between the means for continuous variables was estimated using a two-tailed *t* test.[9] Comparison between clinical, mammographic, and final diagnoses was done using McNemar's test.[10] All possible subset regression analysis was used to identify the "best“ subset variable(s) to predict the presence of breast cancer. The "best“ subset model was selected using Mallows' Cp (coefficient) criterion.[11] All *P* values were two-sided and < 0.05 was considered significant. All data analyses were carried out using 3D, 4F, and 9R programs of the BMDP Statistical Software.[12]

Results

Of a total of 509 mammographic studies, 300 consecutive mammograms were considered evaluable. These were done between 1983 and 1988 in 300 women whose mean age (± SD) was 36.11 ± 11.2 years (range, 14 to 72 years). There were 196 (65%) Saudi and 104 (35%) non-Saudi patients. The mean age for Saudis (35.54 years) did not differ from that of non-Saudis (37.24 years) ($P = 0.18$).

The correlation between the initial diagnostic impression and the later review was significantly high. Table 1 shows the distribution of various patients' characteristics, and the clinical, mammographic, and final diagnoses. The final diagnoses were as follows: fibrocystic disease in 177 (59%), invasive carcinoma of the breast in 26 (9%), and fibroadenoma in 24 (8%). The remaining 73 patients (24%) had no abnormality. Of the

TABLE 1. *Characteristics and clinical, mammographic, and final diagnoses in 300 patients.*

	Final diagnosis [No. (%)]				
Variable	Normal (N = 73; 24%)	Carcinoma (N = 26; 9%)	Fibrocystic disease (N = 177; 59%)	Fibroadenoma (N = 24; 8%)	Total
Age (y)					
≤30	20(20)	7(7)	60(60)	13(13)	100
31–50	47(26)	12(7)	111(62)	9(5)	179
>50	6(29)	7(33)	6(29)	2(9)	21
Nationality					
Saudi	51(26)	16(8)	114(58)	15(8)	196
non-Saudi	22(21)	10(10)	63(60)	9(9)	104
History of lump					
Yes	51(25)	23(11)	104(52)	24(12)	202
No	22(22)	3(3)	73(75)	0(0)	98
Mastalgia					
Yes	28(25)	5(4)	75(68)	3(3)	111
No	45(24)	21(11)	102(54)	21(11)	189
Clinical diagnosis					
Normal	69(58)	2(1.5)	47(39)	2(1.5)	120
Carcinoma	2(2)	24(25)	65(68)	4(4)	95
Fibrocystic	2(3)	0(0)	55(95)	1(2)	58
Fibroadenoma	0(0)	0(0)	10(37)	17(63)	27
Mammography					
Normal	71(100)	0(0)	0(0)	0(0)	71
Carcinoma	0(0)	26(79)	4(12)	3(9)	33
Fibrocystic	2(1)	0(0)	171(99)	0(0)	173
Fibroadenoma	0(0)	0(0)	2(9)	21(91)	23

26 patients with breast cancer, 23 had invasive ductal carcinoma and three had invasive lobular carcinoma. Film mammography was ordered for screening for early cancer detection in only two non-Saudi patients (aged, 40 and 45 years) and one Saudi patient (aged, 35 years). All three women were asymptomatic and clinically free but had a family history of breast carcinoma. A negative final diagnosis was rendered in all three. The remaining 297 (99%) were seen because of symptoms. The mean duration of awareness of a breast lump in the cancer patients was 8.04 ± 2.11 (SD) months (range, 1 to 36 months) compared to 5.61 ± 0.78 months (range, 1 to 60 months) in the others but this difference was not significant *(P = 0.29)*. Conversely, cancer patients had a shorter mean ± SD duration of mastalgia (2.5 ± 0.5 months) compared with that for other patients (6.42 ± 1.11 months) ($P = 0.0019$). Twenty-three patients were seen because of nipple discharge.

The incidence of breast cancer did not differ significantly between those women younger than 30 years and those between 31 and 50 years of age. However, women older than 50 years showed a 33% incidence (7 of 21 patients) in the present study population. Also noted was the significant difference in the mean ± SEM age in the cancer victims (44.08 ± 3.06 years) compared to that for others (35.38 ± 0.62 years) ($P = 0.0097$). Fibrocystic disease predominantly affected young and middle age groups. Fibroadenomas were identified in two women aged 62 and 65 years, respectively. Analysis of various diagnoses failed to show any significant difference between Saudis and non-Saudis.

Of the 26 patients with carcinoma of the breast, only two (7.7%) had Stage I disease. Of the remaining 24 patients, nine (34.6%) were in Stage II, ten (38.5%) were in Stage III, and five (19.2%) were in Stage IV. All detected neoplasms were invasive. All 177 patients with fibrocystic disease, including the 47 patients without clinical abnormality, had histological confirmation. Proliferative fibrocystic disease without atypia was found in 171 patients (97%) and atypical hyperplasia was diagnosed in six (3%).

As shown in Table 1, comparison between the final and the most likely clinical diagnosis showed a significant concordance ($P < 0.0001$). Similarly, a significant correlation between the final and the mammographic diagnosis was also noted ($P = 0.027$). As shown in Table 1, the specificity and sensitivity of mammography were 79% and 100%, respectively, and the accuracy of the procedure was estimated at about 89%.

The all subset regression analysis was carried out to identify the independent factor, or factors, that could predict the probability of breast carcinoma. All covariates shown in Table 1 were used. Mammographic diagnosis was found to be the only factor that was able to predict that a certain woman possessed a high probability of breast cancer. Results of the regression model are shown in Table 2 ($r^2 = 0.698$).

Discussion

The diagnostic value of mammography in various breast diseases has been known for many years.[1,2] The current retrospective analysis of 300 mammographic studies revealed details about female breast disorders in a group of women seen at a tertiary care facility in Saudi Arabia. While the data may not reflect the national or regional pattern, because our hospital has the only unit in the region, our sample is therefore not highly selective.

Invasive carcinoma of the breast was identified in 8% of the Saudi women and 10% of the non-Saudis; 27% of the patients were younger than 30

TABLE 2. *All-possible subset regression analysis for predicting the presence of breast cancer.*

Variable	Regression coefficient	SE*	t-statistic	2-tailed P value	Mallow's C_p	Model P value
Intercept	0.2857	0.0267	10.68	< 0.0001		
Mammographic diagnosis of breast cancer	0.7142	0.0278	25.70	< 0.001	–2.64	< 0.0001

SE = standard error.

years of age. Another 46% of the neoplasms occurred in patients aged 31 to 50 years. Breast cancer patients were significantly older than those who were either normal or had benign breast disease. The mean duration of awareness of a breast lump prior to diagnosis exceeded 8 months, and this delay in seeking medical advice is probably the reason why about 60% of the patients presented with Stage III and IV disease. Early breast cancer (i.e., Stage I) was diagnosed in only 7.7% of all victims of the disease. These observations are compatible with the general impression about breast cancer in the Kingdom, namely relatively young age at presentation, delay in seeking help, and late stages at diagnosis.[8]

Fibroadenoma was the final diagnosis in 8% of all women. It was found in only two women over 50 years of age and this small incidence is in keeping with a recent report that showed the average age of patients with fibroadenoma is 50 years.[18]

Mammograms were done because of symptoms in 99% of the women, indicating that neither local practicing physicians nor women at risk are aware or convinced of the importance of screening mammography. The American Cancer Society recommends that, in addition to regular breast and physical examinations, a baseline mammogram should be obtained in all women between the ages of 35 and 39 years with subsequent mammograms taken every 1 to 2 years in women aged 40 to 49 years and every year in women aged 50 years and older.[13] Reluctance in following these guidelines was also noted among primary care physicians in the United States. In a recent survey, only 11% of American physicians were found to follow the Society's recommendations.[13]

In our series, film mammography proved to be an effective diagnostic tool. It produced 100% sensitivity, 79% specificity, and 89% accuracy. These high rates could be attributed to the fact that all patients were examined and their mammographic studies evaluated by the same senior radiologist (A.Y.E.) with the help of only one senior resident (F.A.A.). Conversely, the small number of cancer patients in our study might also have contributed to these high rates. Multiple regression analysis showed that mammography was the only independent factor which accurately predicted carcinoma. Despite its shown value and its known low risk for radiation-induced cancer,[14] screening mammography should be proposed in the Kingdom only after careful definition of the population at risk. The cost-benefit ratio of an indiscriminate screening program could be enormous.[15]

In our series, 59% of the mammographic studies revealed evidence of fibrocystic disease. The incidence in Saudi (58%) and non-Saudi (61%) women was comparable. In our series, the ratio between proliferative disease without atypia and atypical hyperplasia was almost 29 to 1 (171 and six patients, respectively). Significantly lower ratios were reported from two recently published studies; 7.4 to 1[16] and 2 to 1.[17] These differences may be partially due to patient selection. It was recently shown that the relative risk of cancer for women with proliferative disease without atypical hyperplasia is 1.9 times that in women with nonproliferative lesions.[16] Furthermore, the risk in women with atypical hyperplasia was 5.3 times that in women with nonproliferative lesions, and the coexistence of family history raised that relative risk to 11 times.[16] These recent data should be taken into consideration if a mammography screening program is launched in the Kingdom.

Despite clinical normality, breast biopsy was performed in 47 patients who proved to have fibrocystic disease. In 41, the retrospective review could not pinpoint the reasons for recommending biopsy as there was clear mammographic evidence of fibrocystic changes. Biopsy done in the remaining six patients disproved the erroneous mammographic diagnosis of carcinoma in four patients and fibroadenoma in two.

Mammography is an important and indispensable diagnostic tool that can influence decision-making in the management of breast disorders and not infrequently overrule clinical impression. Our retrospective review of 300 consecutive mammograms has revealed several observations. The diagnostic reliability of film mammography and its significant concordance with final diagnosis was clearly shown in our analysis. We are concerned about the finding that only 1% of women underwent mammography for screening and that the remaining 99% of the women were symptomatic, most for a significantly long period. The observed pattern of breast disease in our series should be compared with that from other health care facilities in the Kingdom. Health care deliverers need to assess physician and patient awareness about breast diseases and the value of screening mammography, and future planning for a national breast cancer early detection program must be undertaken.

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MANAGEMENT OF DISLOCATED HIP IN PATIENTS WITH FITTKE-TYPE CONGENITAL CUTIS LAXA

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هناك نوع مغاير نادر من تهدل الجلد الولادي وصفه (فتكة) يترافق بخلع الورك الولادي. وقد تم الإبلاغ عن ١٨ حالة بينها عشرة سعوديين. قد يفشل علاج هذه الحالات بسبب خلل النسيج الضام، ولكن واقع خبرتنا مع ١٢ طفلاً تظهر إمكانية معالجة هذه الحالات وتحقيق نتائج جيدة.

A rare variant of congenital cutis laxa first described by Fittke is associated with congenital dislocation of the hips. A total of 18 cases have been reported, ten of which occurred in Saudis. Treatment can fail because of the underlying soft tissue abnormality, but our experience in 12 children demonstrates that such patients can be treated with good results.

Congenital cutis laxa is an unusual familial condition that affects a mixed group of patients.[1] While the most common form (inherited as an autosomal dominant) is benign and is frequently discovered later in life, a second form (inherited as an autosomal recessive) is associated with severe systemic malformations that are commonly fatal within the first year. A subgroup of this recessive variant form first, described by Fittke,[2] is often associated with congenital dislocated hips. Of 18 cases reported, ten occurred in Saudis.[3] None of the reports,[3-7] however, discussed the management of the dislocated hips.

A child with dislocated hips who has an underlying soft-tissue disorder might be expected to fail orthopedic treatment, and two patients early in our series were denied treatment on this basis. Subsequent findings, described here, however, demonstrate that such children can be treated with good results.

Patients

Between June 1979 and September 1988, 12 children were seen with Fittke-type congenital cutis laxa and unstable hips. Patient age at the time of the first visit varied between 4 days and 10 years. There were ten girls and two boys. Follow-up in the seven patients who underwent treatment ranged from 6 to 72 months (average, 35 months) (Table 1).

One patient who had bilateral dislocated hips was first seen when she was 10 years old. At that time her family was told that her hip condition was untreatable because she was too old, regardless of her cutis laxa. Two patients, aged 3¼ and 4½ years when first seen, were not treated because the orthopedic surgeon anticipated that the hips would redislocate because of the soft-tissue defect.

Four patients were treated by closed reduction. Of these, two children had traction prior to the closed reduction (one for two weeks and one for three weeks). Two of the children treated by closed reduction subsequently required proximal femoral rotation osteotomies. Normal hips have developed in four children without the complication of avascular necrosis.

Three children had hips that were located but dislocatable when first seen. All were treated: one in a Von Rosen splint, one in an Ilfeld splint, and one in a Pavlik harness. Normal hips have developed in all.

One child with subluxated hips and another with located but dislocatable hips received no treatment. Both children now have normal hips.

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Table 1. *Summary of patients.*

Age at diagnosis	Sex	Hip diagnosis*		Treatment†	Age at last visit	Outcome
		R	L			
3 mo	F	D/R	D/R	T–no; CR SC × 3 m AB × 7 m	12 m	Normal
3 mo	F	D/U	L/D	T–no; CR SC × 3 m AB × 7 m	22 m	Normal
6 mo	M	D/U	D/U	T × 2 w; CR SC × 5 m AB 1 mo FO at age 2	60 m	Normal
16 mo	F	D/U	D/U	T × 3 w; CR SC × 3 m FO at age 2	42 m	Normal
4 d	F	D/R	D/R	Von Rosen × 6 m	60 m	Normal
Birth	F	L/D	L/D	AB × 5 m	60 m	Normal
1 wk	F	S	L/D	Pavlik 3 m	6 m	Normal
Birth	F	L/D	L/D	None	17 m	Normal
4 m	F	S	S	None	19 m	Normal
3¼ y	F	D/U	D/U	None	11 y	Dislocated
4½ y	M	D/U	D/U	None	4½ y	Dislocated
10 y	F	D/U	D/U	None	10 y	Dislocated

* DU = dislocated/unrelocatable; D/R = dislocated/relocatable; L/D = located/dislocatable; S = subluxated.

† = traction; CR = closed reduction; SC = spica cast; AB = abduction brace; FO = femoral osteotomy.

Discussion

Congenital cutis laxa with dislocated hips is a rare disease, with many cases occurring in Saudi children. Treatment, when done in such children, has led to the formation of normal hips in all, based on both clinical and x-ray findings.

Orthopedic surgeons are ordinarily pessimistic about the success of treating a dislocated hip when there is an underlying soft-tissue abnormality but this concern is unfounded. Such children should undergo the same treatment used for otherwise normal children who have congenitally dislocated hips.

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DEVIATED NASAL SEPTUM IN SAUDI NEWBORNS

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بلغت نسبة الأطفال المصابين بانحراف الوتيرة ٧,٢٪ من بين ٥٠٠ طفل ولدوا في مستشفى القوات المسلحة . وتبين بنتيجة الاختبارات التي أجريت على مختلف المتغيرات الجنينية والأمومية لمعرفة مدى تأثيرها على حدوث إنحراف الوتيرة الولادي أن مدة المرحلة الثانية من المخاض كانت المتغير الوحيد الذي له علاقة هامة بانحراف الوتيرة. كما أظهرت النتائج أن هناك عوامل أخرى عدا رضح الولادة يمكنها إحداث إنحراف الوتيرة الولادي (ونعني بها عوامل الحمل) .

Of 500 Saudi infants born at the Security Forces Hospital in Riyadh, 7.2% were found to have deviated nasal septum. Different fetal and maternal variables were tested for their influence on the incidence of congenital deviated septum, and duration of the second stage of labor was the only variable found to be significantly associated with septal deviation. Results showed that factors other than labor trauma could produce congenital deviated nasal septum (i.e., pregnancy factors).

Deviated nasal septum could be due to traumatic or developmental causes. Since Metzenbaum[1] first described deviated nasal septum in the newborn, trauma during labor has been recognized as a possible cause. The reported incidence of congenital deviated nasal septum varies. Metzenbaum[1] reported 1%, Cottle et al,[2] 10%, and Alpini et al,[3] 6.3%. Gray[4] discovered a slight degree of nasal septal deviation in 58% of all newborns studied. This variation could be attributed to different study design, but racial factors could also be involved. Because of this and as no such studies have been conducted in Arabs, we undertook to assess the incidence of deviated nasal septum in Saudi newborn babies, and to correlate it with fetal and maternal variables.

Subjects and Methods

From June 1988 to January 1989, 500 Saudi infants born at Security Forces Hospital were evaluated for septal deviation. They were examined by anterior rhinoscopy using an otoscope and Gray's method.[4] In the latter method, a 4-mm-wide and 2-mm-thick Silastic strut is inserted into each nostril after being lubricated. The strut is pushed along the floor of the nose, hugging the septum. Normally, the strut can be introduced for 4 to 5 cm but arrest of the strut at 1.5 to 2 cm indicates obstruction due to septal deviation.

The medical records of all mothers and infants were examined for the following variables: parity, delivery route, instrumentation, fetal position, duration of second stage of labor, infant sex, and birth weight. The significance of these variables in relation to the occurrence of septal deviation was studied by the chi-square test and significance was defined at $P \leqslant 0.05$.

Results

Of the 500 neonates, 36 (7.2%) had septal deviation. Among the mothers, 110 were primipara and 390 multipara, and septal deviation was found in 10% (N = 11) and 6.4% (N = 25) of their infants, respectively. There was no significant difference between the two groups ($P = 0.2$; $X^2 = 1.65$). Of 269 male infants, 19 (7.06%) showed septal deviation compared with 17 (7.36%) of 231

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female infants. The sex of the infant was not significantly associated with septal deviation (*P* = 0.09: X^2 0.02). To assess the effect of birth weight on the incidence of deviated nasal septum, the infants were divided into three subgroups. Of 52 low-birth-weight babies (< 2.5 kg), four (7.69%) had septal deviation. Of 320 babies whose birth weight fell between 2.5 kg and 3.5 kg, 24 (7.5%) had deviated septums. In the high-birth-weight group (> 3.5 kg), eight (6.25%) of 128 infants had deviated nasal septums. When the three groups were compared, birth weight was not found to be significantly associated with deviated nasal septum (*P* = 0.9; X^2 = 0.02).

Vaginal delivery in 418 mothers yielded 33 babies with deviated septum (7.89%), while three of 82 infants (3.66%) delivered by cesarean section had septal deviation, but this did not achieve statistical significance (*P* = 0.17; X^2 = 1.84). Because of the insufficient number of infants delivered with forceps (six of 418 vaginal deliveries), statistical analysis of this variable could not be done.

The most common fetal presentation was occipitoanterior; of 397 babies, 30 (7.56%) had deviated nasal septum. Other presentations included brow, face, and occipitoposterior. Of 21 such presentations, three infants (14.28%) had deviations. This difference between the two groups was also not statistically significant (*P* = 0.18; X^2 = 3.38). The direction of the occipitoanterior presentations was also evaluated, i.e., left versus right. Of 282 left occipitoanterior deliveries, 19 babies (6.74%) had septal deviation compared with 11 (9.57%) of 115 right occipitoanterior deliveries. There was no statistically significant difference seen with the direction of internal rotation (*P* = 0.50; X^2 = 0.47). The remaining 82 infants were delivered by cesarean section, therefore they were not included in the analysis of this birth variable.

Second stage of labor, commencing from the time of full cervical dilation until delivery, ranged from 2 to 100 minutes. Subjects were divided into three subgroups based on the following durations: less than 15, 15 to 30, and more than 30 minutes. The incidence of deviated nasal septum increased with prolongation of the second stage of labor and was 5.76%, 11.49%, and 16.6% in the three groups, respectively. This difference among the groups was statistically significant at *P* = 0.03 (X^2 = 7.2).

Discussion

The frequency of deviated nasal septum in Saudi newborns in this study (7.2%) is comparable to that observed in different Western populations, thus eliminating racial factor as a likely influence. Because different pregnancy and labor mechanisms that may cause trauma to the infant's nose are essentially similar among different races, this further rules out race as a significant variable.

Duration of the second stage of labor was the only factor that was significantly associated with the frequency of deviated nasal septum in newborns. During this time of labor, maximum parturition pressures are exerted to expel the fetal head and the soft cartilaginous nose is subjected to trauma. Because the second stage of labor is generally more prolonged in primiparas than in multiparas, an increased incidence of deviated nasal septum would be expected in the offspring of the former; however, this was not seen in our series. One study did show an increased incidence of deviated septum among primiparas, but in their population, multiparas had a longer second stage.[3] Most studies conclude that the length of the second stage of labor is an important variable.

If labor contractions were a main causative factor, fetal presentation would have proved to be a significant variable. During face and brow deliveries, the infant's nose is subjected to more direct trauma and this would be expected to lead to a higher incidence of septal deviation. A higher incidence would also be expected following right occipitoanterior presentation because the arch of internal rotation is longer than that with left occipitoanterior presentations. In neither event was an increased incidence of deviated nasal septum seen in our study. The fact that congenital septal deviation occurred in babies delivered by cesarean section also disproves labor contraction as a cause of nasal trauma. This suggests that deviation could happen during pregnancy.[7] Long sustained pressure against the nose caused by the fetus's hand or a uterine fibromyoma can produce nasal deviation.[8]

Developmental rather than traumatic factors could also be involved. Abnormal development of the palatal folds may cause elevation of the soft palate, thus decreasing the vertical dimension of the nasal cavity and compressing or kinking the septum.[9] Differences in the rate of growth of the septum compared to other midfacial structures could result in a septum that is too large for the space it has to occupy, and consequently it deviates.

Of all the variables investigated, the length of the second stage of labor was the only one that was significantly associated with the incidence of deviated nasal septum in newborns. The possibility of prenatal (pregnancy) causes should also be considered.

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PRAZIQUANTEL, OXAMNIQUINE, AND METRIFONATE IN THE TREATMENT OF SCHISTOSOMIASIS IN RIYADH

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بحثت هذه الدراسة فاعلية عقار برازيكونتال وآثاره الجانبية مقارنة بعقار أوكزامينكوين في علاج مئتي مريض يعانون من الخمج بالمنشقات المنسونية وكذلك مقارنة عقار برازيكونتال بعقار متريفونيت في علاج مئة مريض يعانون من الخمج بالمنشقات الدموية. أعطي عقار برازيكونتال أوكزامينكوين في جرعات مفردة بمعدل ٤٠ مغم/ لكل كغم من وزن الجسم و ٢٥ مغم/ لكل كغم على التوالي. وأعطي عقار متريفونيت في جرعات تعادل ١٠ مغم/ كغم وكرر ثلاث مرات بمعدل مرة واحدة كل اسبوعين. كانت نسبة الشفاء في خمج المنشقات المنسونية ٩٦٪ بعقار برازيكونتال و ٩١٪ بعقار اوكزامينكوين. وبالنسبة للخمج بالمنشقات الدموية كانت نسبة الشفاء ٩٨٪ بعقار برازيكونتال و ٩٠٪ بعقار متريفونيت. كانت الآثار الجانبية عابرة وطفيفة بصفة عامة ولاحظناها في نسبة ٤٤٪ من المرضى الذين عولجوا بعقار برازيكونتال وفي نسبة ٦٠٪ من الذين عولجوا بعقار متريفونيت وفي نسبة ٧٠٪ من الذين عولجوا بعقار اوكزامينكوين. كانت أكثر الآثار الجانبية تواردا الدوار وألم البطن. وخلاصة القول إن هذه العقاقير الثلاثة أثبتت فعاليتها ضد أنواع المنشقات السائدة في منطقتنا. يبدو أن عقار برازيكونتال هو الخيار الأفضل لعلاج المنشقات الدموية، كما أن عقار برازيكونتال وجرعة منخفضة من عقار اوكزامينكوين (٢٥ مغم/كغم) كان لهما نفس التأثير والفاعلية في علاج المنشقات المنسونية.

This study sought to compare the effectiveness and side effects of praziquantel versus oxamniquine in treating 200 patients with *Schistosoma mansoni* infection and praziquantel versus metrifonate in treating 100 patients with *S. haematobium* infection. Praziquantel and oxamniquine were given in single doses of 40 mg/kg body weight and 25 mg/kg, respectively. Metrifonate was given in doses of 10 mg/kg, and repeated three times at fortnight intervals. In *S. mansoni* infections, the cure rate was 96% for praziquantel and 91% for oxamniquine. In *S. haematobium* infections, the cure rate was 98% for praziquantel and 90% for metrifonate. Side effects were generally minor and temporary and were noted in 44% of patients treated with praziquantel, in 60% of patients treated with metrifonate, and in 70% of the patients treated with oxamniquine. The most common side effects were dizziness and abdominal pain. It is concluded that the three drugs are effective against the species of *Schistosoma* present in our area. Praziquantel appears to be the drug of choice for *S. haematobium*. Praziquantel and low-dose oxamniquine (25 mg/kg) were comparable in their effect on *S. mansoni*.

Chemotherapy has become a major component in the control of schistosomiasis since the introduction of effective, safe, and orally administered drugs.[1,2] There are several reports concerning their effectiveness in the treatment of local strains using variable doses, and the reports also describe the features of transmission.[3,4] However, there are only a few reports from Saudi Arabia concerning the use of oral antischistosomal drugs.[5,6] In this study, we report our experience with three

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commonly employed oral antischistosomal drugs in the treatment of *Schistosoma mansoni* and *S. haematobium* infection.

Patients and Methods

Patients with a diagnosis of schistosomiasis based on detection of the parasite's ova in urine and stool samples were referred to the schistosomiasis clinic at King Abdul Aziz University Hospital, Riyadh. Egg output was determined in stool samples using the Kato-Katz technique.[7] In cases of *S. haematobium* infestation, urine was obtained at mid-day and the ova counted in 10 ml of urine after sedimentation.

Proctoscopy was done in those patients who were suspected of having schistosomiasis, but in whom frequent stool examination yielded negative findings. Three rectal specimens obtained during proctoscopy were placed between slides and examined under the microscope. If living ova were seen, the diagnosis of active schistosomiasis was rendered. Only Saudis and Yemenis were included in the study.

One hundred patients infected with *S. haematobium* were allocated randomly to either praziquantel treatment (40 mg/kg of body weight in a single dose; N = 50) or metrifonate therapy (10 mg/kg repeated three times at two-week intervals; N = 50). In addition, 200 patients with *S. mansoni* infection were randomly allocated to either praziquantel (40 mg/kg in a single dose; N = 100) or oxamniquine treatment (25 mg/kg as a single dose; N = 100). Complete clinical examination and investigations included complete blood count, urea and electrolyte determinations, and liver function tests. Patients were then followed for at least 6 months. Cure was determined by the following criteria: clinical improvement and disappearance of ova from urine or stool specimens on three successive examinations, or the presence of dead ova in rectal specimens in cases that were originally diagnosed histologically. The side effects of drugs were recorded at the second visit.

Results

Patient age ranged from 10 to 63 (mean, 26) years and egg output in stool specimen ranged from 1 to 470 ova (mean, 60) per gram. The output in urine ranged from 1 to 500 ova (mean, 75) per 10 ml. Urine findings at 3 and 6 months after treatment are shown in Table 1. At 6 months, the cure rate was 98% for praziquantel and 90% for metrifonate in the treatment of *S. haematobium*. In the treatment of *S. mansoni*, the cure rate was 96% for praziquantel and 91% for oxamniquine.

The adverse effects of the drugs are listed in Table 2. The most common were dizziness (20%, 36%, and 10%) and abdominal pain (12%, 25%, and 12%) for praziquantel, oxamniquine, and metrifonate, respectively. Convulsions occurred in one patient who was treated with oxamniquine.

TABLE 1. *Results of stool and urine examination 3 and 6 months after treatment.*

	Positive cases from urine examination		Positive stool examination	
Drug	3 mo	6 mo	3 mo	6 mo
Praziquantel	4%	2%	6%	4%
Metrifonate	12%	10%	–	–
Oxamniquine	–	–	11%	9%

TABLE 2. *Percentage of patients' complaints related to antischistosomal drugs.*

Symptoms	Praziquantel	Oxamniquine	Metrifonate
None	56	30	40
Dizziness	20	36	10
Abdominal pain	12	25	12
Joint pain	10	12	10
Nausea	8	10	6
Rash	6	4	2
Vomiting	6	10	8
Itching	6	10	–
Fatigue	2	12	8
Hair loss	2	–	–
Change in taste	1	2	2
Diarrhea	1	2	4
Convulsion	–	1	–

Discussion

Praziquantel represented an advance in the treatment of schistosomiasis. In our study its use led to a high cure rate for *S. mansoni* (96%) and *S. haematobium* (98%). In the treatment of *S. man-*

soni infection, Katz et al[8] performed the first clinical trials in adult patients using doses of 20 mg/kg, given three times, and 50 mg/kg, given once, and the cure rate was over 90%. Other workers found a cure rate between 94%[9] and 97%.[10]

In *S. haematobium* infection, McMahon[11] observed a cure rate of 90% and egg output reduction of 99%, while Pugh et al[12] reported a cure rate of 90%. In other studies the cure rate at six months varied between 83% and 100%.[10] We observed a 90% cure rate in patients with *S. haematobium* infection who were treated with metrifonate, and this is comparable to the rates reported in other studies.[12-13] Oxamniquine in different dosages has been used in different parts of the world to treat schistosomiasis.[14,15] The cure rate in our study was 91%. El-Mallah[5] and Al-Aska[6] have used it in cases occurring in Saudi Arabia. The dosage they used was 20 to 30 mg/kg with subsequent cure rates of 97.6% in El-Mallah's cases and 88% in Al-Aska's patients. A report from Brazil notes an 80 to 95% cure rate in adult patients given an oral dose of 15 mg/kg. Higher doses have been reported to yield lower cure rates in some African countries.[14-17]

In our study, 44% of the patients treated with praziquantel suffered side effects (Table 2). In their study in a Brazilian population, Katz et al[8] found that 57% of adults and 74% of children treated with a similar dosage sustained side effects, the most common being abdominal distress. Strickland et al[17] reported side effects in 60 to 79% of their patients.

Side effects were seen in a higher proportion (70%) of our patients treated with oxamniquine and included convulsions in one patient. Katz et al[8] and Lambertucci et al,[18] in Brazil, reported side effects in 35 to 73% and 61% of their patients, respectively, the most common being dizziness and nausea. Most side effects disappeared within 24 hours.

Minor side effects were encountered in 60% of our patients who took metrifonate, which agrees with findings in other studies.[10,11,13]

We conclude that praziquantel, metrifonate, and oxamniquine in the doses stated are all effective against the schistosomal strains encountered in the Arabian peninsula and that side effects are minor and transient.

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ACUTE NONLYMPHOBLASTIC LEUKEMIA IN ADULTS: EXPERIENCE IN TRIPOLI, LIBYA

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أجرينا دراسة على ٥٤ من المرضى البالغين المصابين بابيضاض الدم الحاد غير اللمفاوي والذي تم تشخيصه خلال خمس سنوات في المستشفى المركزي بطرابلس الغرب، ليبيا. وشملت الأعراض المبكرة في معظم الحالات فقر الدم، الحمى، الحَبَر (النمشة)، والنزف الشبكي. كان مرضانا أصغر سنا (متوسط العمر ٣٤ عاماً) وكان المرض في مرحلة أكثر تقدماً وقت المعاينة الأولى مقارنة بما يشاهد في الغرب. تلقى ٣٧ مريضاً التحريض بمعالجة كيميائية تشتمل على «سايتوزين أرابينوسايد»، و «دونوروبيسين»، و «٦ - ثيوغوانين». تحققت هدأة تامة للمرض في ١٥ حالة (٤٠٪)، مع بقيا وسطية قدرها ٤٠ أسبوعاً. كما تحققت هدأة جزئية في ١١ حالة أخرى (٣٠٪)، وتوفي ١٧ مريضًا قبل البدء بالمعالجة الكيميائية. كانت النتائج الإجمالية بعيدة المدى ضعيفة بشكل عام. وكان خمج الدم والنزف داخل الجمجمة من أكثر أسباب الوفاة. وقد واجهتنا صعوبات عملية في إجراء عمليات زرع الطعم الذاتي والمثلي لنقي العظام بسبب اضطرارنا إلى إحالة المرضى إلى الخارج. يجب تحسين الامكانيات والوسائل اللازمة لعلاج مرضى إبيضاض الدم الحاد.

We conducted a study of 54 adult patients with acute nonlymphoblastic leukemia that was diagnosed over a 5-year period at Central Hospital, Tripoli, Libya. The majority of patients presented with anemia, fever, petechiae, and retinal hemorrhages. Our patients were younger (median age, 34 years) and the disease was more advanced at the time of presentation than that seen in the West. Thirty-seven patients were given induction chemotherapy comprising cytosine arabinoside, daunorubicin, and 6-thioguanine. Fifteen patients (40%) achieved complete remission, with a median survival of 40 weeks. There was partial remission in another 11 patients (30%), and 17 patients died before chemotherapy was begun. Overall long-term results were generally poor. Common causes of death were septicemia and intracranial hemorrhage. There were practical difficulties in carrying out autologous and allogenic bone marrow transplantation, as patients had to be referred abroad. Facilities for treating patients with acute leukemia need to be improved.

Acute nonlymphoblastic leukemia (ANLL) is a relatively uncommon disease and presents commonly with anemia, fever, and bleeding. Until about ten years ago, the condition was rapidly fatal; complete remission was achieved in about 20% of the cases and median survival was less than six months.[1] Over the last few years, high remission rates of between 60 and 92% have been reported following the judicious use of combination chemotherapy comprising daunorubicin (an anthracycline antibiotic), cytosine arabinoside (a pyrimidine analogue), and 6-thioguanine (a purine analogue).[2-6] These regimens are severely myelotoxic and intensive care in the form of blood component therapy and broad-spectrum antibiotics is required during the period of hypoplasia. The overall long-term survival in patients is about 25% and most suffer relapse within two years of

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remission.[7] Relapses are generally fatal as they are refractory to chemotherapy. Allogenic bone marrow transplantation during first remission has been helpful in offering prolonged disease-free survival and possible cure.[8]

We discuss our experience with ANLL in adult patients seen between January 1981 and March 1986 at Central Hospital, Tripoli. This is the largest referral hospital in western Libya, which has a population of about two million.

Patients

Clinical and Laboratory Features

Sixty-six adult patients were diagnosed to have ANLL, representing about 4% of all cancer patients registered in this hospital. Complete records were available for 54 patients and only these patients were included in the study. Patients with chronic myeloid leukemia in blast crisis were excluded. Patients were treated in the hematology unit and all patients were cared for in isolation rooms. Laminar flow facilities were not available.

Diagnosis was based on the morphological features of peripheral smears and bone marrow aspirates using Romanowsky stains. Cytochemical staining—myeloperoxidase, Sudan black, and periodic acid-Schiff—was done in all patients and subtyping was done according to FAB classification (Table 1).[9] There were 32 male and 22 female patients. The age range was 14 to 77 years with a median of 34 years (Table 2). The common clinical features were anemia (80%), weakness and fatigability (66%), bleeding (54%), and fever (34%), alone or in combination. Splenomegaly (40%) and lymphadenopathy (30%) were also seen, while bone pain (15%) and gum hyperplasia (11%) were seen in a minority of patients. Three patients were diagnosed during pregnancy, two of whom aborted, and one had a full-term normal delivery. One more patient was diagnosed on the twentieth postpartum day, when she presented with septicemia after home delivery. A 28-year-old woman was diagnosed three months after receiving postoperative radiotherapy for breast cancer. Retinal hemorrhages were seen in about half of the patients and only two patients presented with an overt central nervous system (CNS) disease or cranial nerve paralysis. Two patients presented with life-threatening upper gastrointestinal hemorrhage due to ulcerations that were confirmed by endoscopy. One patient presented with acute renal failure, gout, and hyperuricemia. Four patients presented with disseminated intravascular coagulation. The median duration of symptoms before diagnosis was seven weeks.

TABLE 1. *Type of leukemia in the 54 patients based on FAB classification.*

Type	Number
M1, undifferentiated myeloblastic	4(7%)
M2, differentiated myeloblastic	31(57%)
M3, promyelocytic	8(15%)
M4, myelomonocytic	7(13%)
M5, monocytic	2(4%)
M6, erythroleukemia	2(4%)

TABLE 2. *Age distribution of 54 patients with acute nonlymphoblastic leukemia.*

Age (y)	Number
14–20	3
21–30	11
31–40	18
41–50	10
51–60	5
61–70	5
Above 70	2

Treatment

The induction and maintenance chemotherapeutic regimens employed are given in Table 3.[6] Only 37 patients were given induction chemotherapy. The other 17 patients were not given chemotherapy as they had a poor WHO performance status of 4. Drug dosages were reduced to 75% of the calculated doses because blood component therapy was difficult to obtain. Two induction courses were given at 3-week intervals. Bone marrow examinations were done in the third week after the second induction course to confirm remission. All patients received prophylactic co-trimoxazole and allopurinol. Severe prolonged pancytopenia developed in all patients. This confirmed adequate drug dosages. Patients who had clinical signs of septicemia were intensively monitored by repeated throat swabs and cultures of

TABLE 3. *Chemotherapy: TAD regimen—modified dose and route of administration.*

Drugs	Dose	Day	Route
Induction			
Cytosine arabinoside	75 mg/m^2	1–7	Subcutaneously, 6-hourly
6-Thioguanine	75 mg/m^2	1–7	Orally
Daunorubicin	40 mg/m^2	5–7	Intravenously
Maintenance (continue until relapse)			
1st month:			
Cytosine arabinoside	100 mg/m^2	1–5	Subcutaneously, 8-hourly
Daunorubicin	60 mg/m^2	1	Intravenously
2nd month:			
Cytosine arabinoside	100 mg/m^2	1–5	Subcutaneously, 8-hourly
6-Mercaptopurine	100 mg/m^2	1–5	Orally
3rd month:			
Cytosine arabinoside	100 mg/m^2	1–5	Subcutaneously, 8-hourly
Vincristine	2 mg	1	Intravenously
Prednisolone	40 mg/m^2	1–5	Orally

TAD = thioguanine, cytosine arabinoside, daunorubicin.

sputum, blood, and urine. Broad-spectrum antibiotics (cephalosporine, gentamycin, and carbenicillin) were administered either alone or in combination.

Results

Eleven (30%) of the 37 patients who underwent chemotherapy did not respond and died within four weeks of induction. There was partial remission in 11 patients (30%), as judged by the increase in hemoglobin content and platelet count, and about a 50% reduction in the blast count in bone marrow aspirates. The median survival in these patients was 16 weeks. Two patients, one M2 and the other M6, went into partial remission and one survived for 34 weeks after diagnosis. Induction chemotherapy, using the same regimen, was continued in all these patients until death. Fifteen patients (40%) went into complete remission and had a median survival of 40 weeks. The median age of the patients who went into remission was 27 years. Of these, five patients were referred for allogenic bone marrow transplantation abroad. In others, it was not done either because of advanced age or nonavailability of matched donors. Three patients referred abroad for allogenic bone marrow transplantation died during the procedure and two patients were lost to follow-up. Ten patients (7 males and 3 females) with a median age of 27 years were put on maintenance chemotherapy and all suffered relapse. The median duration of remission and survival in these patients was 38 and 60 weeks, respectively. One patient relapsed four times and died 110 weeks after diagnosis. Three other patients had remissions twice. None of the patients with M1 or M6 disease went into complete remission. This may be due to the small number of patients in these groups and not necessarily indicate a bad prognosis for this type of disease. All six patients who presented with pancytopenia and were treated died early and none went into complete remission. The patient who had irradiation for breast cancer and developed ANLL tolerated chemotherapy poorly and died within four weeks of starting chemotherapy. Common causes of death in those who relapsed were septicemia in 25 (46%), intracranial hemorrhage in 9 (16%), or both in 8 (15%). Other causes were acute renal failure in two (4%) and disseminated intravascular coagulation in six (11%). Four patients (9%) were alive at the time of this report. Intensive search for a causative organism in the 33 patients who had septicemia was positive in only 12 (*Staphylococcus aureus* in seven, *Klebsiella pneumoniae* in three, and *Pseudomonas aeruginosa* in two). The side-effects of chemotherapy in most patients included nausea, vomiting, and alopecia. Cardiotoxicity was seen in two patients who were on maintenance chemotherapy and had received cumulative doses of 650 mg and 580 mg of daunorubicin, respectively.

Discussion

Our experience with ANLL, which consists of the largest collection of cases in Libya so far, has shown that the features exhibited by adults in western Libya resemble those observed in the West, except that the median age of our patients (34 years) was younger and the disease was more advanced at the time of diagnosis, as indicated by the severity of the anemia and the thrombocytopenia.[10,11] The cause of early occurrence of disease in Libyan patients is not clear and could be due to unknown genetic factors or the younger median age of the population. The reasons for the more advanced disease at diagnosis could be the low health awareness among the rural population, late diagnosis, and referral from outlying hospitals. The response to treatment was better in younger patients than in the elderly, and this agrees with findings of other observers.[6,12] Patients presenting with leukopenia did not respond.

Drugs effective in the treatment of ANLL cause bone marrow aplasia that lasts for about two weeks.[13] During this period, patients require intensive care in the form of isolation, blood component therapy, and intensive monitoring and treatment for infection. As many as 40 to 70% of patients may die during this period.[14] Our remission rate of 40% is low compared to those reported in other series.[2-6] This could be due to the more advanced stage of the disease in our patients and complications at the start of treatment as well as the nonavailability of blood component therapy. The long-term median survival in our patients was comparable to those reported elsewhere and is generally poor.[15] Maintenance chemotherapy was given to ten patients with fair results, although limitations were imposed by daunorubicin-induced cardiotoxicity. Most patients suffered relapse within one year, and therefore allogenic bone marrow transplantation should be considered early. Even though it was considered desirable for the young patients in first remission, it could not be done in most because either matched donors were not available or appropriate referral centers abroad could not be found in time. Clinically, overt CNS disease was seen in only 4% of our patients at presentation, but a large number died of intracranial hemorrhage. Prophylactic CNS treatment was not carried out, as its role in ANLL is not firmly established.[6] Seventeen patients (30%) died before effective treatment could be given. This forms a large group and some of these patients could have been treated. This emphasizes the need for improved health consciousness, early diagnosis, and prompt referral. The hematology and blood component services need to be improved and facilities for autologous and allogenic marrow transplant need to be developed locally.

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CLINICAL FEATURES AND MORTALITY OF ACUTE MYOCARDIAL INFARCTION IN BENGHAZI, LIBYA

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تم تحليل جميع حالات احتشاء عضلة القلب الشديد بين الليبين الذين أدخلوا إلى وحدة العناية الاكليلية بين ٠١ كانون ثاني/ يناير و ٣١ كانون أول/ ديسمبر ١٩٨٦م، فيما يختص بنسبة الوقوع وعوامل الخطر المصاحبة وأنماط الاحتشاء واضطرابات النظم والإحصار والاختلاطات المتعلقة بحركية الدم والوفيات داخل المستشفى. استوعب نظام الرعاية الصحية الواسع ببنغازي جميع الحالات تقريبًا. كانت نسبة الوقوع خلال السنة المذكورة ٧٣ لكل ١٠٠,٠٠٠ من السكان الذين تبلغ أعمارهم ٤٠ عامًا فما فوق: ١١٢ للرجال و ٣٠ للنساء من كل ١٠٠,٠٠٠. ويعتبر هذا الرقم منخفضًا جدًا اذا قورن بما يقابله في البلدان المتقدمة. كان أكثر عوامل الخطر شيوعًا التدخين لدى الرجال والسكري لدى النساء. وكانت نسبة وقوع إضطرابات النظم اجمالاً (اضطراب النظم والتوصيل) ٨٧,٥٪. أما إحصار القلب التام فقد لوحظ لدى ١٠٪ من الحالات. وحدثت الصدمة قلبية المنشأ لدى ٦,٣٪ وكانت نسبة الوفيات في المستشفى ٢٠٪.

All cases of acute myocardial infarction among Libyans admitted to the coronary care unit (CCU) from January 1 to December 31, 1986, were analyzed regarding incidence, associated risk factors, infarction patterns, arrhythmias, blocks and hemodynamic complications, and in-hospital fatalities. The extensive health care system of Benghazi ensured nearly complete inclusion of cases. The one-year incidence of 73 per 100,000 population for those aged 40 years and older was 112 for men and 30 for women per 100,000. This figure is very low compared to that for developed countries. The most common associated risk factor was smoking in males and diabetes mellitus in females. The overall incidence of arrhythmias (including disturbance of rhythm and conduction) was 87.5%. Complete heart block was observed in 10% of the cases. Cardiogenic shock occurred in 6.3%, and in-hospital mortality was 20%.

Coronary artery disease is the most frequent cause of mortality and morbidity in the world, and myocardial infarction (MI) is the most dreaded manifestation of the disease. Most data about the clinical and epidemiologic aspects of MI come from developed countries. Because of scanty data from developing countries, it is difficult to make comparisons with the data from developed countries.[1]

The present study records and analyzes the data about acute myocardial infarction and its occurrence over a period of one year in Libyan patients living in Benghazi, the second largest city of Libya.

Methods

The population of Libyans in Benghazi in 1986 was 565,000. The city is situated in the northeastern part of Libya on the southern Mediterranean coast. The inhabitants are of mixed Arab, African, Turkish, and South European descent. There are two major university hospitals, six polyclinics,

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and many dispensaries. Medical treatment is free and no system of private medical practice exists. Hospital and/or a private means of transport is available to all. All suspected cases of acute coronary events are referred to the six-bed coronary care unit (CCU) based at the Seventh of April Hospital.

All patients with acute unequivocal MI who were of Libyan nationality and admitted to the CCU from January 1 to December 31, 1986, were included in the study. Patients with old silent myocardial infarction, acute coronary insufficiency, angina pectoris, re-infarction within the study period, and referrals from outside Benghazi City were excluded, as well as those who died suddenly of the MI. MI was diagnosed in the presence of diagnostic Q waves, evolutionary ST waves, T wave changes, and/or appropriate serum enzyme changes. The data were analyzed with respect to age, sex, prevalence of various risk factors in each sex, the type and location of the infarction and the occurrence of various arrhythmias, conduction disturbances, and hemodynamic aberrations. In-hospital mortality was also examined in relation to various clinical parameters.

Risk factors analyzed included hypertension, diabetes mellitus, hypercholesterolemia (serum cholesterol > 5.70 mmol/L), smoking habits, previous infarction, obesity, and oral contraceptive use. The arrhythmias and conduction disturbances were diagnosed on the basis of continuous monitoring records obtained during the patients' stay in the CCU. Hemodynamic aberrations like left ventricular failure cardiogenic shock were diagnosed on the basis of clinical and, in some instances, radiologic findings. Overall in-hospital mortality was determined from hospital records of patients. Incidence was calculated based on Libyan population figures obtained from the 1973 and 1984 national censuses. The 1986 population was extrapolated from the growth rate occurring between 1973 and 1986.

Results

In the one-year study period, 80 cases of acute MI were recorded among Libyan nationals living in Benghazi. There were 64 males (80%) and 16 females (20%). Age range for males was 38 to 76 years (mean age, 57.05 ± 10.3 SD) and for females, 43 to 80 years (mean age, 62.5 ± 14.2 SD).

The incidence of acute MI for patients 40 years and older was 73 per 100,000 population. The incidence for males and females in the same age group were 112 and 30 per 100,000, respectively.

Specific age and sex incidence rates are given in Table 1. In males, the rates gradually increased with age except in the seventh decade. Eleven of 16 (70%) females were 60 years or older.

Prevalence Risk Factors

Risk factors and their prevalence in the study group are outlined in Table 2. Among males, smoking was the most prevalent risk factor (68.7%), followed by history of previous angina (37.5%), obesity (34.3%), diabetes mellitus (31.2%), hypertension (17.1%), and previous MI (12.5%). There were no smokers among the females and diabetes mellitus was the most prevalent risk factor (62.5%), followed by hypertension, obesity, and hypercholesterolemia and pre-

TABLE 1. *Age and sex specific incidence of acute MI in Libyans in Benghazi in 1986.*

Age (y)	Male Population	Male No. of cases	Male Incidence /100,000	Female Population	Female No. of cases	Female Incidence /100,000	Total Population	Total No. of cases	Total Incidence /100,000
<30	208,247	0	0	198,538	0	0	406,785	0	0
30–39	26,229	3	11	27,103	1	4	53,332	4	8
40–49	21,993	11	50	20,786	3	15	42,779	14	33
50–59	13,361	19	142	11,989	1	9	25,350	20	79
60–69	4,028	22	546	4,680	3	64	8,708	25	288
70 +	15,168	9	59	12,735	8	63	27,903	17	61
All ages	289,026	64	22	275,831	16	6	564,857	80	14
<40	54,550	61	112	50,180	15	30	104,730	76	73

TABLE 2. *Prevalence of various risk factors in acute MI cases.*

	Males (N=64)		Females (N=16)		Total (N=80)	
Risk factor	Total no.	%	Total no.	%	Total no.	%
Previous angina	24	37.5	6	35.5	30	37.5
Previous infarction	8	12.5	1	6.3	9	11.3
Smoking	44	68.7	0	0	44	55
Hypertension	11	17.1	8	50	19	23.7
Diabetes	20	31.2	10	62.5	30	37.5
Hypercholesterolemia	8	12.5	6	37.5	14	17.5
Obesity	22	34.3	6	37.5	28	35
Oral contraceptive	–	–	1	6.3	1	1.3

TABLE 3. *Occurrence of arrhythmias in acute MI cases with their relationship to mortality.*

	Occurrence		Mortality	
Arrhythmias	No. of cases	%	No. of cases	%
Significant ventricular ectopics	29	36.5	6	20.7
Paroxysmal supraventricular tachycardia	1	1.3	–	–
Atrial fibrillation	4	5.0	1	25
Accelerated idioventricular rhythm	2	2.5	–	–
Ventricular tachycardia	7	8.8	3	42.9
Ventricular fibrillation	7	8.8	5	71.4

TABLE 4. *Occurrence of conduction defects in acute MI cases with their relationship to mortality.*

	Occurrence		Mortality	
Conduction defects	No*	%	No.	%
LAH	3	3.8	–	–
LPH	1	1.3	–	–
LBBB	2	2.5	1	50.0
RBBB	3	3.8	2	66.6
Bifascicular block (RBBB + LAH)	1	1.3	1	100.0
I° heart block	7(6)	8.8	1	14.8
II° heart block	5(5)	6.3	–	–
III° heart block	8(7)	10.0	1	12.5

*Number in parentheses indicates the number of cases with inferior wall infarction. The rest of the cases were anterior wall infarction.

LAH = left anterior hemiblock; LPH = left posterior hemiblock; LBBB = left bundle branch block; RBBB = right bundle branch block.

vious angina (each 37.5%). One 33-year-old woman with hypertension had used oral contraceptives for 10 years. She suffered an extensive anterior acute myocardial infarction and died of cardiogenic shock. Seven patients (8.8%) did not have any associated risk factor (three males and four females).

Type and Location of MI

Of the 80 cases of acute MI, 62 patients (77.5%) had transmural infarction; of them, 50 patients were male and 12 were female. The remaining 18 patients (22.5%) had subendocardial infarction (13 males and 5 females). Extensive anterior infarction was the most common (40%), followed by anteroseptal (30%), inferior (25%), and lateral (5%) wall infarction.

Arrhythmias, Conduction Disturbances, and Hemodynamic Complications

Significant ventricular arrhythmias included frequent ventricular premature beats (VPBs) in pairs, runs of less than five VPBs, ventricular bigeminy, VPBs with R on T waves, and multiple VPBs. Arrhythmias were recorded in 36.5% of our cases; of them 20.7% died. The second most common arrhythmias were ventricular tachycardia (8.8%) and ventricular fibrillation (8.8%) with a mortality of 42.9% and 71.4%, respectively. Of the total 16 deaths, 11 patients had had some kind of arrhythmia (Table 3).

Complete heart block was the most common conduction disturbance and was observed in eight (10%) patients. Of these, seven had inferior infarctions. All the cases of second-degree block actually had varying heart block between the first and third degree. Pure first- and third-degree heart blocks were seen in two and three cases, respectively. In our series, only one patient with complete heart block died, and he had extensive anterior infarction (Table 4).

Left ventricular failure was diagnosed in 17 (21.3%) patients and almost a third of these patients died (35.3%). Cardiogenic shock occurred in five cases (6.3%) with an 80% mortality.

Mortality

In-hospital mortality for all cases of acute MI was 20% (16 deaths): 12 were male (18.7%), four were female (25%). Eleven of 16 deaths occurred in patients above the age of 60 years, signifying higher mortality with advancing age. Death was attributed to various arrhythmias and conduction and hemodynamic disturbances (see Tables 3 and 4). Cardiogenic shock was the cause of death in four cases (25%).

On relating mortality to the time of CCU admission, the highest mortality (37.5%) was recorded in the first six hours. Two (12.5%) patients died in the next 18 hours. Three patients (18.8%) succumbed on the second and third day and two (12.5%) died between four to seven days after their MI. Three patients (18.8%) died during the second week of their hospital stay.

Discussion

An extensive and free medical and health care system, freely available transportation, ample public awareness of heart disease, and only one CCU in the city are factors that ensure inclusion of the maximum numbers of acute MI cases in our series. Sudden deaths, nonreferred doubtful cases, and sociocultural beliefs that discourage hospital care, especially in the elderly, could account for some cases being omitted. Because of the nearly complete data for acute MI, along with population figures, determination of the incidence of acute MI in Benghazi should be fairly accurate.

Despite the small study size, some established epidemiologic trends were evident. There was a male preponderance for each age group, except those patients about 70 years of age. Incidence rose with age up to the seventh decade. The low incidence in the eighth decade could be due to the reluctance of elderly to seek hospital care (Table 1).

The one-year incidence of acute MI in Benghazi in 1986 in patients 40 years old and up was 73 per 100,000 population. Moussa et al[2] computed this to be 143 per 100,000 population for the year 1984 in the Benghazi area. The difference is statistically significant ($P < 0.001$). This higher incidence in 1984 could be due to inclusion of acute MI cases referred from nearby areas of the city, which were excluded from the present series. Wide periodic, geographic, seasonal, and racial variation in the incidence and prevalence of coronary artery disease are known to occur.[3,4] The data from these two years are inadequate for determining the trends of occurrence of acute MI in the defined population.

On comparing our data with that from developed countries, the incidence of acute MI in the Libyan population is found to be very low.[5-7] The relative rarity of coronary artery disease in Africans is well recognized. Among Nigerians, the necropsy incidence of MI in all autopsies is reported to be 0.01%,[8] while 71% of coronary arteries studied histologically showed no evidence of atherosclerosis.[8] In South African whites the rate of coronary artery disease matched well with Western figures, while it remains an uncommon finding in blacks.[9] In eastern Africa it is a major cause of death in only those of Indian origin.[9]

The overall incidence of arrhythmias (including disturbance of rhythm and conduction) in our study was 87.5%. In developed countries the incidence of such disorders in acute MI patients treated in a CCU ranges between 62 and 96%.[10,11] The average incidence according to representative studies is 85%,[12,13] which is comparable to our figures.

In the present study, the incidence of significant VPBs was 36.5%, which compares well with those reported by Mogensen[11] (32%) and Lowrie et al[14] (42%). The mortality of our patients in this group was 20.7%. The incidence of atrial fibrillation in various reports has ranged from 7 to 20%.[11,13] In our series it was recorded in 5% of the cases.

We defined ventricular tachycardia as six or more consecutive VPBs at more than 120 beats per minute. The incidence in our series was 8.8%, which compared well with the 10% cited by Meltzer and Kitchell.[13] Despite treatment for the tachycardia, the mortality for this arrhythmia was reported to be as high as 40 to 50%.[15] In our series the mortality was 42.9%.

Ventricular fibrillation occurs in approximately 10% of patients treated in CCUs.[13,14] In the present study it occurred in seven (8.8%) cases with mortality in five (71.4%). Cardiogenic shock in one case and advanced cardiac failure in five cases may be considered to have contributed significantly to the occurrence of ventricular fibrillation as well as an unfavorable response to cardioversion.

Most monitored series indicate that complete heart block develops in 5 to 8% of patients with acute MI.[12,14] In our series it was observed in eight (10%) cases. Of these, seven patients had inferior infarction and one with anterior infarction died.

The incidence of left ventricular failure in patients with acute MI at the time of admission varies between 24 to 63%.[16,17] The associated mortality varies between 17 to 48% in these series. In our series, the incidence (21.25%) was low but the mortality (35.3%) compared well.

The real incidence of cardiogenic shock in acute MI has been confused by lack of consistent definition of the term. In our study, we defined cardiogenic shock as whenever blood pressure fell below 90 mm Hg, plus two of the following clinical criteria were met: (1) dulled sensorium; (2) cold peripheries; and (3) urine output lower than 20 ml/hour. Cardiogenic shock was recorded in 6.25% of our cases, with 80% mortality. Klauss et al[18] reported the presence of hypotension alone in 12% of the cases while true cardiogenic shock occurred in 11%.

The in-hospital death rate in our series (20%) compared well with the figures reported from Britain[19] (19%) and Kuwait[20] (18%).

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CLINICAL EXPERIENCE WITH DIABETIC PREGANCY IN RIYADH: ANALYSIS OF 357 CASES

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يعرض هذا المقال تحليلاً لثلاثمائة وسبع وخمسين (٣٥٧) امرأة حامل مصابة بالسكري راجعن العيادة المشتركة للحمل والسكري (الرياض، المملكة العربية السعودية). كان خمس وثمانون بالمئة (٨٥٪) منهن يعانين من سكري الحمل (الفئة أ من تصنيف وايت) وخمس عشرة بالمئة (١٥٪) من السكري السابق للحمل (الفئة ب وج من تصنيف وايت). لزم العلاج بالأنسولين لمئة واثنتي عشرة امرأة (٢٩٪) وفيهن ٤٩ من المصابات بسكري سابق للحمل، في حين أمكن ضبط السكري لدى الأخريات بالحمية فقط. كان إجمالي نسبة العمليات القيصرية ١٣٪، وكان ذلك ذا أهمية إحصائية بدرجة خاصة في مجموعة المصابات بسكري سابق للحمل (P < 0.001). ووجدت ضخامة الجسم (تجاوز الوزن ٤ كغم) لدى ٦٣ وليدًا (١٨٪) ونقص سكر الدم (غلوكوز الدم أقل من ٢,٢ ميلليمول/لتر) لدى ٧٠ (٢٠٪). أما الشذوذات الجنينية الخلقية الرئيسية فكانت موجودة لدى تسعة ولدان (٢,٥٪)، وكان ذلك ذا أهمية إحصائية لدى مواليد المصابات بالسكري السابق للحمل (P = ٠,٠٣٨). ويضم المقال مقارنة بين المجموعات المختلفة والاجراءات المقترحة لتحسين النتائج في مجتمعنا.

An analysis of 357 pregnant diabetic women attending the pregnancy-diabetic combined clinic (Riyadh, Saudi Arabia) is presented. Eighty-five percent were gestational diabetics (White's class A) while 15% were pre-gestational diabetics (White's class B and C). One hundred and twelve (29%) women required insulin, including 49 women with pre-gestational diabetes. The diabetes in others was controlled with diet alone. Overall cesarean section rate was 13%, and this was significantly high in the pre-gestational diabetic group *($P < 0.001$)*. Macrosomia (birth weight > 4 kg) was present in 63 neonates (18%) and hypoglycemia (blood glucose, < 2.2 mmol/L) in 70 (20%). Major congenital fetal anomalies were present in nine (2.5%) of the neonates and this was significantly high in those infants born to pre-gestational diabetics *($P = 0.038$)*. Comparison is made between the different groups and measures to improve the outcome in our community are suggested.

Dramatic improvement has been achieved in perinatal mortality among pregnant diabetic women,[1,2] and this has been synonymous with maternal education, early and strict control of blood glucose levels, and obstetrical surveillance. The findings on pregnancy complicated by diabetes have been mainly reported from Western countries. We report on our clinical experience from Riyadh, Saudi Arabia, concerning 357 diabetic pregnancies.

Material and Methods

Analysis of 304 completed pregnancies in women with gestational diabetes (White's class A) and 53 patients with pre-gestational diabetes (White's class B and C) is reported. All patients were followed at the Obstetrical Diabetic Clinic at

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King Abdul Aziz University Hospital in Riyadh. All pregnant women (except pre-gestational diabetics) underwent routine screening for abnormal glucose values following a 75-gm glucose load. Blood glucose levels of 7.8 or higher were considered abnormal and this led to performance of a glucose tolerance test[3,4] (i.e., fasting and two hours after a 75-gm glucose load). The criteria adopted for screening and diagnosis of gestational diabetes followed those recommended by WHO in 1985.[3,4]

Women with pre-gestational diabetes (White's class B and C) were all started on a diet or on insulin and diet regimen to maintain fasting blood glucose at 4 mmol/L and a 2-hour post- and preprandial level below 7 mmol/L. This was determined following admission of women to the hospital for initial serial blood glucose evaluations and ophthalmic, renal, and other vascular assessment, with further admissions as necessary for blood glucose evaluation (fasting and 2-hour postprandial blood glucose evaluation done on outpatient basis) or development of obstetrical complications. When possible, glycosylated hemoglobin (HbA_{1c}) was measured monthly, but patient compliance was poor. The means and standard deviations of HbA_{1c} levels are shown in Table 1.

TABLE 1. *Maternal characteristics.**

Variables	White's class A	White's class B and C	*P* value
Age (mean ± SD)	30.3±5.3 yr	31.7±5.5 yr	0.1
Age > 30 yr	175(57%)	35(66%)	0.1
Parity			
Primiparous	34(11%)	2(4%)	
1–4	156(51%)	26(49%)	
5	114(38%)	25(47%)	
Gestational age at presentation			
First trimester	57(19%)	29(55%)	
Second trimester	93(30%)	13(25%)	
Third trimester	154(51%)	11(20%)	
Overweight (> 120%)	189(62%)	25(47%)	>0.05
HbA_{1c}	7.2% ± 1.29 (N = 120)	8.43% ± 131 (N = 44)	
Mode of delivery			< 0.001
Vaginal	276(91%)	35(66%)	
Cesarean section	28(9%)	18(34%)	
Hypertension	29(10%)	7(13%)	> 0.1

White's class A = gestational diabetes mellitus; White's class B and C = pre-gestational diabetes; HBA_{1c} = glycosylated hemoglobin.

*Statistical significance was determined by Student's *t* test, the Mann-Whitney U test, and Yate's correction.

All gestational diabetic women were cared for on an outpatient basis. Initially their diabetic status was assessed by fasting and 2-hour postprandial blood glucose estimation. Patients were admitted if the fasting and the 2-hour postprandial glucose levels were more than 6 and 8 mmol/L, respectively. Further management followed guidelines similar to those for pre-gestational diabetics. Again, patient compliance was poor. Antenatal care was provided by the obstetrical clinic. If no complications developed and blood glucose levels were satisfactory, both on outpatient and inpatient basis, pregnancy was allowed to continue to term. Induction of labor or elective cesarean section were considered on an individual basis by the obstetrician in charge. Newborns were assessed by Apgar score at 1 and 5 minutes and for birth weight, hypoglycemia (< 2.2 mmol/L), hypocalcemia, and other neonatal complications. Congenital abnormalities were recorded as major (life-threatening) or minor (non-life-threatening). Gestational diabetic mothers were advised to have a glucose tolerance test at 6 weeks postpartum. However, the majority did not attend and therefore this information is lacking from our data.

Maternal features such as age, parity, weight (overweight = 120% of ideal body weight), blood pressure, status and treatment of diabetes, and mode of delivery were compared between the pre-gestational and gestational groups. Similarly, the newborns of both groups were studied for low Apgar score (< 7), birth weight, hypoglycemia (blood glucose, < 2.2 mmol/L), and congenital anomalies.

Significance was measured by Student's paired *t* test and the Mann-Whitney U test with Yate's correction. $P < 0.05$ was considered statistically significant.

Results

Table 1 summarizes the maternal characteristics of the gestational (White's class A) and pre-gestational (White's class B and C) diabetic women. The overall mean age ± standard deviation for both study groups was 30.4 ± 5.4 years;

TABLE 2. *Newborn characteristics.**.

Variables	White's class A	White's class B and C	P value
Preterm (<37 weeks GA)	14(4.6%)	2(3.8%)	–
Birth weight (kg, mean ± SD)	3.48 ± 0.48	3.48 ± 0.68	>0.5
Birth weight > 4 kg	49(16%)	14(26%)	>0.05
Apgar < 7			
at 1 min	40(13%)	8(15.1%)	>0.5
at 5 min	2(1%)	3(5.7%)	>0.5
Hypoglycemia	54(17.8%)	16(30%)	<0.005
Congenital malformation			0.038
Minor	10(3%)	1(2%)	
Major	5(0.01%)	4(8%)	

*Statistical significance was determined by Students' *t* test, Fisher's exact test, and Yate's correction.

†Overall perinatal mortality rate, 8.4/1000 deliveries. White's class A = gestational diabetes mellitus; White's class B and C = pre-gestational diabetes.

TABLE 3. *Summary of major and minor fetal congenital anomalies.*

Patients	Anomalies	
	Major	Minor
White's class A*	Hypoplastic left ventricle, 1††	Undescended testes, 3
	Intestinal obstruction, 1	Talipes, 1
	Exomphalos, 1	Extra digits, 1
	Ventriculomegaly, 1	Hydrocele, 1
	Down's syndrome, 1	Unknown, 3†
White's class B	Anencephaly, 1††	
	Multiple anomalies, 1††	
	Tetralogy of Fallot, 1	
	Rectovaginal fistula, 1	

*Major anomalies were 2.5 times more prevalent in pre-gestatonal diabetics.

†Anomalies were not described but identified only as minor.

††Died.

White's class A = gestational diabetes mellitus; White's class B and C = pre-gestational diabetes.

57% and 66% of the women were over 30 years of age in the gestational and pre-gestational diabetic groups, respectively. There was no significant difference between the two groups regarding age, parity, or the development of hypertension during pregnancy. Significantly more pre-gestational diabetics were managed earlier in pregnancy than were gestational diabetics. More pre-gestational diabetics required insulin (92%) and more underwent cesarean section (34% versus 9%), while only 21% of the gestational diabetics required insulin in addition to dietary control. In those patients whose HbAlc levels were tested, the mean (± SD) levels in patients treated only with diet was 8.06 ± 1.46% (N = 73) and those treated with diet and insulin, 7.31 ± 1.13% (N = 85). Data on the pre-gestational weight were not available for either group; however, there were more overweight women (> 120% of ideal weight) in the gestational than pre-gestational diabetic group, but this did not achieve statistical significance.

Newborn characteristics are given in Table 2 and detailed description of congenital anomalies in Table 3. The mean (± SD) birth weight for all babies was 3.48 ± 0.50 kg. There was no statistical difference between the two diabetic groups with regard to birth weight, Apgar score, macrosomia (> 4 kg birth weight), or preterm delivery (prior to 37 weeks' gestation). Hypoglycemia developed in more babies born to pre-gestational diabetic mothers than in gestational diabetic mothers (30% versus 18%), but this was statistically significant ($P < 0.005$).

The incidence of major anomalies in neonates was significantly greater (2.5 times) in the pre-gestational diabetic group compared to the gestational diabetic group (Fisher's exact test, $P = 0.038$). Initial HbA_{1c} levels were not recorded for infants with congenital anomalies. The perinatal mortality rate for both groups was 8.4/1000 deliveries. Because of the small number of minor congenital abnormalities recorded for both groups of infants, no conclusions could be drawn concerning the rate of occurrence. HbA_{1c} levels are unknown for women early in the first trimester because patients were seen late in the first or second trimester.

Discussion

The findings in the present study clearly support the large body of evidence in the literature of improved results from diabetic pregnancies,[1,2,5,6] but fetal congenital anomalies still account for the majority of perinatal deaths.[2] In this study, major congenital anomalies accounted for two perinatal deaths in the pre-gestational diabetic group. In both instances the mothers presented for treatment late in pregnancy. During the study period, only 59% of the confirmed pre-gestational diabetics started appropriate therapy. If the occurrence of congenital malformations in the offspring of diabetic mothers is to be reduced, pre-conception counseling and control are necessary.[6,7] White's class A diabetes is usually found in four to fivefold of gestational diabetics.[1] A 6.6-fold incidence was found in the present study. This higher incidence is attributed to our use of WHO criteria, which led to our including in the gestational group those patients with impaired glucose tolerance. The prevalence of abnormal glucose tolerance in our patients is about 9%.[4]

A blood glucose level of between 4 to 7 mmol/L is the recommended limit for satisfactory control[6,8] and we tried to meet this in our patients. Home monitoring of blood glucose levels by patients was tried in a small number of cases and the results were encouraging. HbA_{1c} measurement has been used to monitor diabetic control, but does not replace the information derived from intermittent blood glucose measurements.[6] HbA_{1c} is the subject of an ongoing prospective study of diabetes in pregnancy and outcome. In the present study, HbA_{1c} levels were not determined on a regular basis, since most patients presented late in pregnancy and were noncompliant in performing the test.

As expected, a significantly high number of our patients (92%) with pre-gestational diabetes required insulin. Seventeen percent of our gestational diabetic patients required insulin which agrees with figures cited in another report.[9] The need for cesarean section was also significantly greater in the pre-gestational diabetic group than the gestational group, and this also agrees with the findings of other studies.[5,10] There were more overweight women in the gestational diabetic versus the pre-gestational diabetic group.[4] No other differences were observed between the two groups in terms of maternal characteristics.

Twenty-six percent of the infants born to pre-gestational diabetics weighed 4 kg, compared to a 16% prevalence in the gestational diabetic group, but this difference was not statistically significant. Lavin et al[10] reported similar findings. Eighteen percent of the infants born to mothers in our study were macrosomic, and this is twice the 9% seen overall for infants born in our obstetrical unit. Macrosomic infants born of diabetic mothers indicates poor diabetic control, and the incidence seen in our study may be attributed to late recognition of diabetes as well as poor control.[2,4,11]

The significant number of fetal abnormalities in infants born to pre-gestational diabetics corroborates other findings,[2,12] and has been attributed to disturbance of maternal metabolism during embryogenesis.[7] Pre-conception diabetic control should lead to reduced congenital abnormalities and thus improved perinatal mortality and morbidity.[6,8]

Conclusion

Early recognition and follow-up are the primary goals in our patient population, and this can be achieved through health educators stressing to diabetic women the need to regularly attend diabetic clinics to achieve control of their diabetes prior to conception. Early and regular prenatal care, screening of the entire pregnancy population for gestational diabetes, stringent control of blood glucose levels throughout pregnancy, obstetrical surveillance, and postnatal follow-up are also essential. An important approach to the care of diabetic mothers is the establishment of a pregnancy diabetic clinic where specialists in obstetrics and diabetes as well as nurse educators can work as a team in the care of these patients. The 9% rate of abnormal glucose tolerance seen in the pregnant women in our community[4] emphasizes the need to establish such services.

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A FAMILY WITH BILATERAL DUANE'S RETRACTION SYNDROME, DOMINANT INHERITANCE, AND PROMINENT SYSTEMIC FEATURES

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أصيب ستة أفراد من عائلة واحدة بمتلازمة دوين المتميزة بتراجع المقلة. وتصف هذه المقالة انتقال
المتلازمة كصفة موروثة سائدة وأبرز الملامح الجهازية، بالاضافة إلى أسباب هذا المرض.

Six members of one family were affected by Duane's retraction syndrome. Its dominant mode of inheritance and prominent systemic features are described, along with the etiology of the disorder.

Duane's retraction syndrome was first described by Stilling[1] in 1887 and Turk[2] in 1896. The syndrome is characterized by limitation or absence of abduction and/or adduction of the eyes. There is also retraction of the globe and narrowing of the palpebral fissure on adduction which is often associated with elevation or depression of the globes. When abduction is attempted, one often finds widening of the palpebral fissure. Duane[3] in 1905 emphasized that retraction of the adducted involved eye is an essential feature of this syndrome.

The possible etiology of the syndrome, i.e., the role of inheritance in its acquisition and its frequent association with musculoskeletal anomalies, make it an interesting entity. It affects more females than males (57%[4] and 64%,[5] respectively). The left eye is more often affected in unilateral cases (67% of the cases versus 23% on the right),[4] and most cases (90%) are sporadic.[6] Approximately 10% of the cases are familial in origin and 30% of the cases have a family history of eye problems.[7]

We will discuss here our findings in a family in which six members were affected by Duane's retraction syndrome.

Material and Methods

A family of English origin was seen in England, in which three generations exhibited ocular and systemic involvement indicative of Duane's retraction syndrome (Figure 1). There was no known consanguinity. Six members of the family were affected; three had bilateral and one unilateral ocular involvement while two had systemic but no ocular involvement (Table 1).

Patient 1

A 3-year-old boy, the child of Patient 4, was first seen because of suspected right convergent strabismus. He had been born two weeks prematurely. Examination revealed his vision was OD 6/9 and OS 6/9 using the Kay test. Ocular movements were markedly limited during adduction and abduction of both eyes, though more pronounced on the left (Figure 2). Convergence was

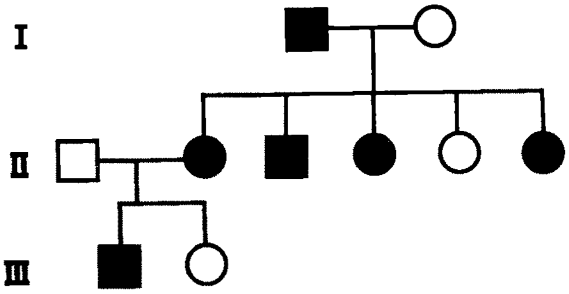

FIGURE 1. Family tree of the affected family. All patients were examined.

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TABLE 1. *Ocular and systemic findings in the reported cases.*

Patient	Age(y)	Sex	Ocular involvement	Systemic involvement
1	3	M	Bilateral	Negative
2	18	F	Bilateral	Brittle bones, kidney problems, cleft palate
3	61	M	Unilateral	Club foot
4	28	F	Bilateral	Extra bone in the right shoulder
5	25	M	Poor convergence	Becker's nevus, cleft palate, hearing problem, deformity of the pinna, deviated nasal septum
6	14	F	Negative	Cleft palate and incisor, fused labia and anomalous genitalia, clicking of the knee and ankle joints

M = male; F = female.

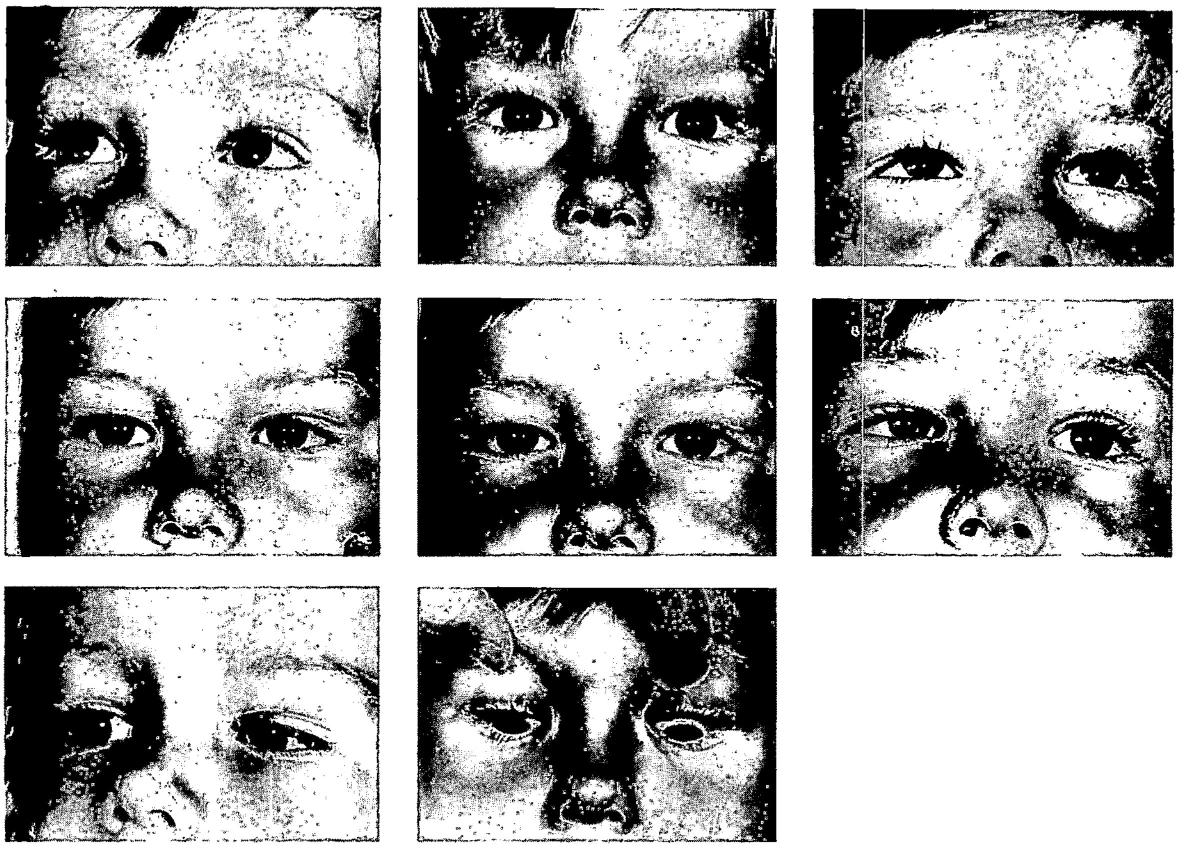

FIGURE 2. Eye movements in Patient 1, showing bilateral involvement.

to 9 cm; however, cover test showed no deviation in the primary position, and no binocular single vision was demonstrated. Refraction testing revealed myopic astigmatism. The patient showed no systemic involvement.

Patient 2

An 18-year-old woman (sister of Patients 4, 5, and 6) with no children was first seen at the eye clinic when she was 5 to 6 years old because of a right divergent strabismus for which corrective

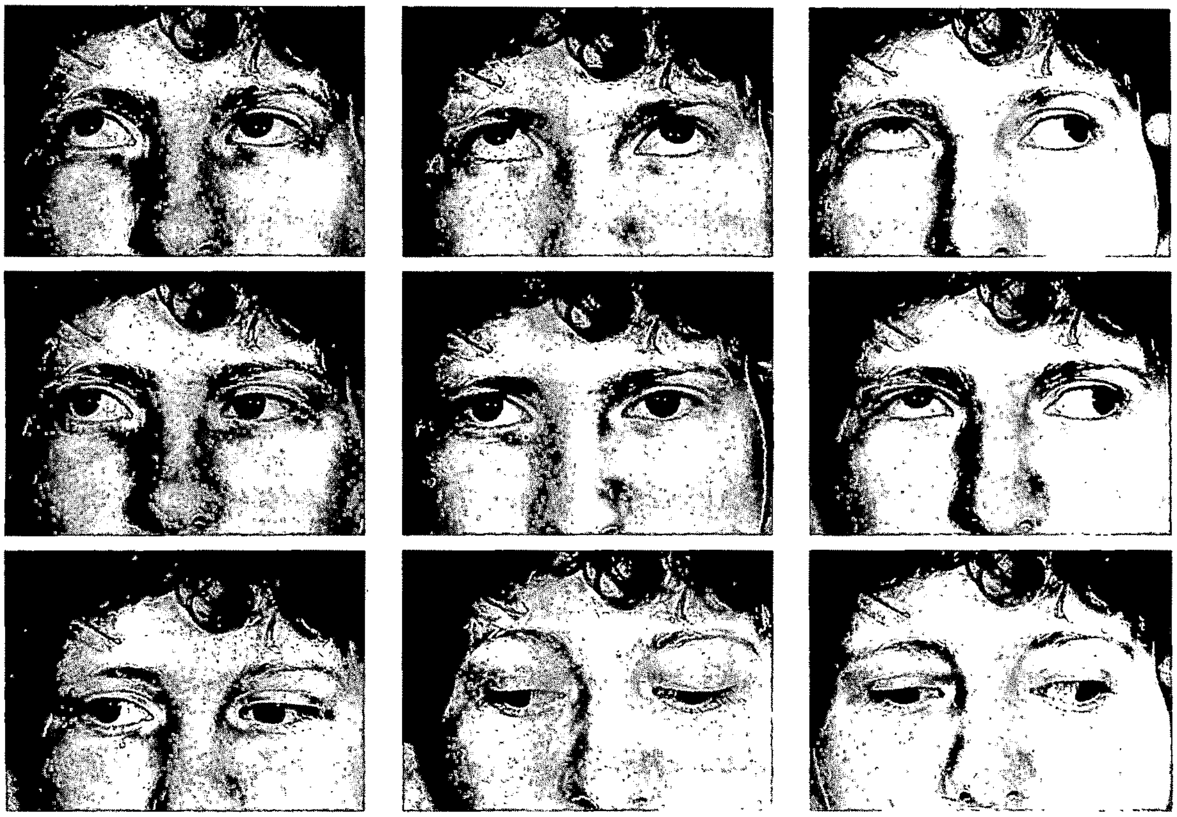

FIGURE 3. Eye movements in Patient 2 who had bilateral involvement with anomalous vertical movement involving the right eye on left gaze.

lenses and occlusion therapy were prescribed. On examination her vision was OD 6/24 and OS 6/5, with correction. Ocular movements in the right eye were markedly restricted more so on adduction than abduction; this was associated with upshoot of this eye on adduction (Figure 3). On fixation there was also some retraction in her right eye that was associated with slight narrowing on depressed adduction. Her left eye also showed restricted adduction but abduction appeared normal. Cover test indicated a slight exotropia in the primary position for near and distance vision, with or without corrective lenses, and this was associated with slight right elevation. The exotropia was marked on downward gaze (i.e., A-exotropia). There was no binocular single vision.

This patient showed systemic involvement; she had brittle bones and kidney problems. She also had a cleft palate that had been repaired when she was 2 years old (Figure 4). The cleft palate was the source of speech problems, for which she attended a special school.

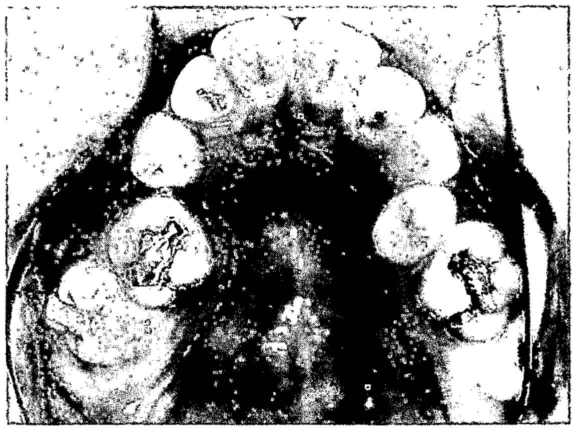

FIGURE 4. Repaired cleft palate in Patient 3.

Patient 3

This patient, a 61-year-old man, and father of Patient 2, 4, 5, and 6, was the first in the family reported to have Duane's retraction syndrome. He had complained all his life of horizontal dip-

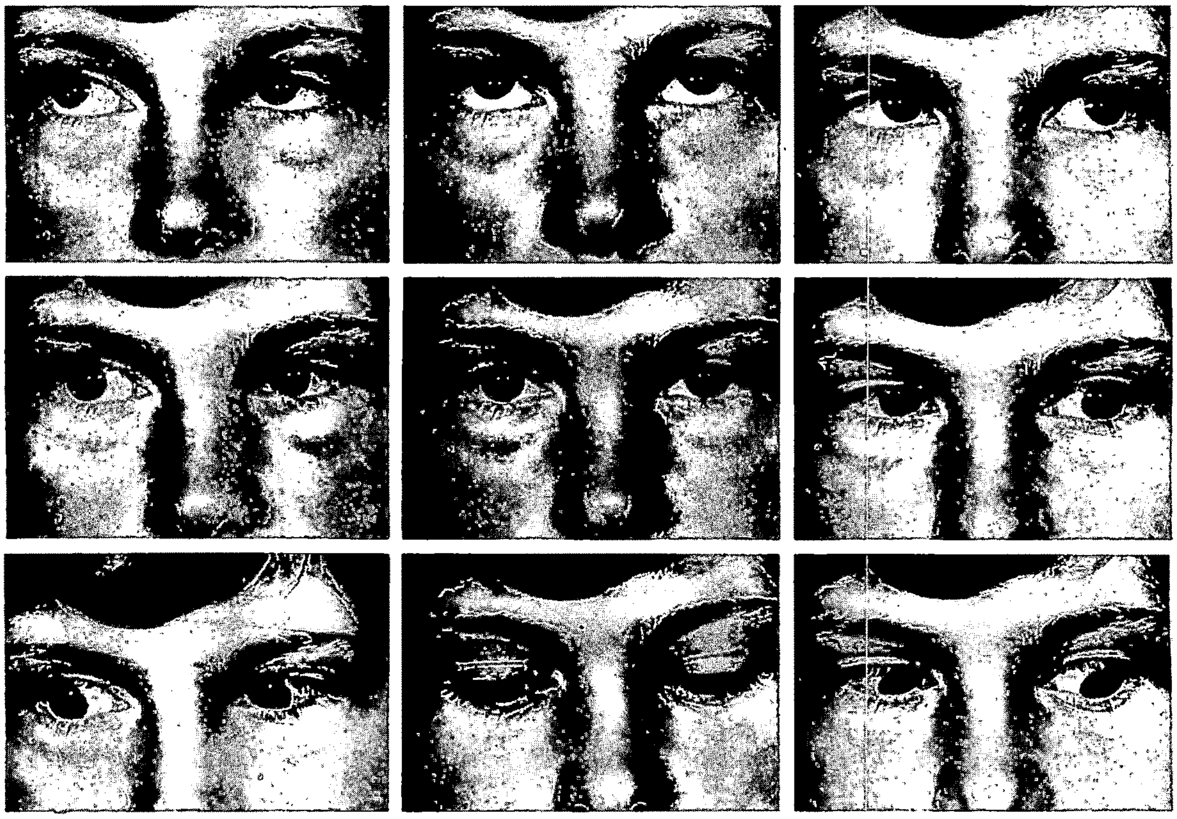

FIGURE 5. Eye movements in Patient 4 showing bilateral restriction on adduction and abduction. This was associated with narrowing of the palpebral fissure on adduction and widening on abduction.

lopia when he looked to the right. Although he had not noticed this in recent years, he did have diplopia on concentration. Ocular movements in the right eye were moderately restricted on abduction and slightly restricted on adduction, with narrowing of the palpebral fissure. The left eye was normal.

The patient's vision was OD 6/4 and OS 6/5 without corrective lenses. There was no ocular deviation for distance vision, but there was an 8 prism diopter exophoria for near vision. The fusion range was small and there was no appreciable diplopia when fusion broke. Additionally there was no demonstrable binocular single vision. The patient had a club foot but no other abnormalities.

Patient 4

The patient, a 28-year-old married woman, is the sister to Patients 2, 5, and 6 and has two children. One was a girl who had no ocular or systemic findings and the other was a boy who is Patient 1. The mother had worn corrective lenses until she was 11 or 12 years old and had also worn a patch on one eye for amblyopia. At the current evaluation ocular movements were noted to be restricted bilaterally on adduction and there was narrowing of the palpebral fissures and retraction of the globe, with the left affected more than the right (Figure 5). There was also bilateral restriction on abduction. Her vision was OU 6/5, without correction. There was slight exophoria with rapid recovery for near and distance vision. Her stereoacuity was 60 seconds. Nonocular findings included the existence of an extra bone in her right shoulder. She had no other congenital anomalies but suffered from stomach ulcer, migraine, and photosensitivity.

Patient 5

This patient, who is brother to Patients 2, 4, and 6, was a 25-year-old single man who had worn corrective lenses since childhood with normal vision. He showed slight exophoria that was associated with poor convergence. He had poor binocular single vision with a stereoacuity of 340 seconds. His ocular movements were otherwise normal.

Aside from the ocular findings, he had a hairy nevus on the back of his left shoulder (Becker's nevus). He also had a cleft palate for which he underwent repair in early childhood. He has had bilateral myringotomies and bilateral antral washout, associated with gross deviation of the nasal septum to the left. At present he complains of discharge and deafness on the left side, and there is a small hemangioma involving the left earlobe. He has anal fissures that are associated with rectal bleeding.

Patient 6

A 14-year-old girl, sister to Patients 2, 4, and 5, had slight exophoria that increased on upgaze. Eye movements were otherwise normal. She had a cleft palate and a cleft incisor for which she had had surgery. She also had a fused labia and anomalous genitalia. In addition, she suffered from clicking of the knee and ankle joints.

Discussion

Duane's retraction syndrome is a heterogeneous disorder that may involve multiple defects and is almost always congenital. Associated congenital anomalies include those of the eyes, skeleton, and ear. The syndrome is also associated with other malformations, including Goldenhar's syndrome, Klippel-Feil syndrome, and familial perceptive deafness (Wildervanck syndrome).

Ocular involvement is variable in severity. Bilateral ocular involvement is seen in from 10%[5] to 18%[4,7] of cases, and asymmetry between the two eyes exists in such cases. Ocular involvement can occur alone or in association with other systemic anomalies, and systemic involvement can occur alone as well.

Systemic malformations occur in approximately 35 to 50% of cases.[4] Various malformations have been described, including skeletal (30%) and ear and hearing (7.5%). One third of the cases have one or more additional malformations, 13% have two or more, and 8% have three or more. Many cases with systemic association have bilateral involvement,[8-10] and such cases tend to be familial. Sevel and Kassar[11] first described bilateral involvement in successive generations.

The present report concerns a family in which six of eight members were involved, and the disease spanned three successive generations. Our cases were characterized by predominantly bilateral ocular involvement. Cleft palate also occurred in three of five patients with systemic involvement. Other anomalies included Becker's nevus, kidney abnormality, skeletal and hearing disorders, deformity of the earlobe, deviated nasal septum, and anomalous genitalia.

The exact cause of Duane's retraction syndrome is still disputed. The frequent association of congenital anomalies suggests that there is a teratogenic stimulus at an early stage of embryogenesis. However, the timing of such events can be pinpointed to the seventh or eighth week of gestation when the hard palate is formed by the fusion of the maxilla, with complete fusion by the eighth to ninth week.[12] In addition, development of the external ear is intrinsically associated with differentiation of the first and second branchial arches and the intervening first pharyngeal groove. These structures appear about the fourth week of gestation, and differentiation into the auricle and external auditory meatus is usually complete by the eighth week.

Regarding the ocular findings, the nuclei of cranial nerves III, IV, and VI appear by about the fourth to fifth weeks of gestation and these nerves reach their respective muscles by the end of eighth week. There is embryologic evidence indicating a common origin of cranial nerves III, IV, and VI, with subsequent segmentation. This may explain why fibers innervating the lateral rectus muscle are incorporated into the main trunk of the third cranial nerve when cranial nerve VI fails to develop.

From all this evidence, the most likely timing of events leading to malformations associated with Duane's retraction syndrome appears to be the second month of gestation.[4,8,13]

Most cases of Duane's retraction syndrome are sporadic and there is a family history in approximately 10%. More than 40 families in which more than one member of the family is affected are described in the literature, and an autosomal dominant inheritance best fits these pedigrees.[10] The gene responsible for Duane's syndrome contains information for bilateral involvement,[14] and appears to be a highly pleiotropic single mutant gene that is frequently nonpenetrant and with great variability of expression.[15]

Some authors believe that cases occurring sporadically are caused by nongenetic factors that operate during early embryogenesis,[16] yet sporadic cases are phenocopies that are indistinguishable from inherited cases. From this one can conclude that a common genetic factor, for both familial and sporadic cases, is operating during the embryogenesis of the affected structures. This gene is inherited in an autosomal dominant pattern, but its penetrance may vary depending on a favorable genetic background or environment. This could explain why most cases of Duane's retraction syndrome are apparently sporadic and noninherited.[14] Additionally, the reduced penetrance of the gene has been encountered frequently and in some cases the disorder is so mild as to be missed.[10] It is certain, however, that in both cases, the events that cause the syndrome occur during the second month of fetal development.

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Special Communication

CADAVERIC ORGAN DONATION IN SAUDI ARABIA

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استنادًا إلى التقديرات على مستوى العالم بوجود ٥٥ حالة يمكن أن تؤخذ منها أعضاء للنقل سنويًا في كل مليون من السكان فإنه يفترض أن يتوفر في المملكة العربية السعودية ٦٦٠ متبرعًا. غير أن المركز الوطني للكلى في المملكة أفاد بأنه تم الحصول على الكلى من ٥٦ متبرعًا فقط خلال سنتين. ولا يمثل هذا الرقم سوى ٤,٢٪ فقط من العدد المفترض توفره من الحالات الممكنة في المملكة، ويقابل ذلك مثلاً بنسبة ١٩,٣٪ في الولايات المتحدة الأمريكية. نجح الأطباء في المملكة العربية السعودية في الحصول على موافقة أهل المتبرع في ٣٧٪ من المحاولات، وهي نسبة تساوي أو تتجاوز النسب الغربية. ومع وصول عدد من يعانون من المراحل النهائية لداء الكلى إلى ٢٠٠٠ تقريبًا في الوقت الحاضر وبدء عمليات نقل القلب والكبد في المملكة فلابد من تركيز الجهود على زيادة عدد الأعضاء المتوفرة لعمليات النقل.

Of the estimated 55 organ donors per million population available worldwide each year, there are a potential 660 in Saudi Arabia, yet the Saudi Arabian National Kidney Foundation reported kidneys retrieved from only 56 donors over a two-year period. This represents only 4.2% of the potential donors within the Kingdom, compared with 19.3% for the U.S.A. Physicians in Saudi Arabia have been successful 37% of the time in obtaining family consent and this is comparable or higher than most Western figures. With the number of end-stage renal disease patients now totaling nearly 2000 and with the advent of heart and liver transplantation in the Kingdom, it is imperative that efforts be concentrated on increasing the number of organs available for transplantation.

Cadaveric organ donation is still in its infancy in the Kingdom of Saudi Arabia. Although more than 100 cadaveric kidney transplants have been performed in the last two years using organs harvested from donors within the country, there is still a large untapped resource of donors. Despite difficulties such as the newness of the program, brain death documentation, and obtaining consent from the large expatriate population, cadaveric kidney transplantation is increasing. The King Faisal Specialist Hospital and Research Centre (KFSH&RC) program has witnessed an almost doubling of the number of transplants in the last two years, from 10 in 1987 to 19 in 1988.

The guidelines that have been established for donor acceptability, donor maintenance, brain death determination, and seeking family permission provide some insight into the process of organ donation for medical professionals. Some difficulties that have been identified with the new program as well as recommendations to help increase the number of organ donors will be discussed.

Background

In 1982 a report of the Senior Religious Leaders Commission (Appendix A) granted approval for both cadaveric and living-related organ donation. In 1986 the Council of Islamic Jurisprudence (Appendix B) formally recognized the declaration of brain death. This acceptance by Islam paved the way for transplantation to be performed within the Kingdom. The KFSH&RC program began with a living-related kidney transplant in 1981.

Unfortunately not all patients who are in need

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of a transplant have a relative who is willing or able to donate. In earlier years, patients without donors were referred abroad to await cadaveric transplantation. This was not an ideal situation as it took the patient away from his or her language, culture, and most importantly, the family support system. With increasing demand, it also became expensive and more difficult for patients to receive transplants abroad. Thus the need for an active cadaveric transplant program within the Kingdom became obvious.

The first two kidney transplants performed at KFSH&RC were done in January 1987 using a cadaver donor referred from the Riyadh Central Hospital. Two teenagers received the organs. Following these initial successes, ten cadaveric kidney transplants were performed in 1987 at KFSH&RC with nine still functioning after one year.

As health officials became aware that successful cadaveric transplantation was a possibility in Saudi Arabia, most patients were no longer referred abroad so that a pool of potential recipients could accrue. Because of the small number of donors referred, some patients grew tired of waiting and chose to go abroad, usually to India, to purchase a living nonrelated kidney. Although sometimes this approach is successful, often such patients return to the Kingdom with more complications than patients who undergo the transplant here. This increased risk to the health of our patients, along with the rising cost of dialysis and difficulty in maintaining qualified personnel, has forced medical professionals to intensify efforts to achieve a more active cadaveric organ donor program.

In 1986, under the auspices of the Ministry of Health, the National Kidney Foundation (NKF) was formed to coordinate dialysis and transplantation. One of its primary goals was to help start an active cadaveric organ donation and transplantation program in Saudi Arabia. The NKF serves as the organ donor referral center for the Kingdom, with all institutions reporting any suitable donors directly to it. It is also responsible for establishing national protocols and guidelines for donor and recipient selection, and also for educating medical professionals and the public about the tremendous need for and benefits of kidney transplantation.

Donor Criteria

The NKF has adopted generally recognized criteria for the acceptance of cadaveric donors, but because of the shortage of donors, some guidelines have been relaxed. These criteria are:

1. Patients with irreversible brain damage on artificial ventilation with maintained respiration and circulation and good renal function.
2. No malignant disease (except primary brain tumor).
3. No systemic infections.
4. No renal disease including chronic hypertension.
5. No generalized vascular disease including atherosclerosis.
6. No donors above the age of 60.

Donors of almost any age are considered, as are diabetics, provided kidney function has not been adversely affected. Sepsis is an absolute contraindication for donation, but localized infections, as indicated by positive sputum or urine culture, are acceptable in the donor. All donors need to be negative for the human immunodeficiency virus. Positive hepatitis B surface antigen donors who are delta antigen negative are acceptable for positive hepatitis B surface antigen recipients. An elevated serum creatinine level is acceptable if it can be demonstrated that rehydration will reverse it. Vasopressor use is not a contraindication to donation. If there is any doubt whether a patient is acceptable, the NKF or a nephrologist at one of the four transplant centers may be consulted, i.e., Riyadh Armed Forces Hospital, Riyadh King Fahad National Guard Hospital, Al-Shaty Hospital in Jeddah, and KFSH&RC.

Donor maintenance is critical to obtaining healthy organs for transplantation and does not conflict with the treatment of the potential donor patient who may be still undergoing assessment of brain death. Kidney function should be preserved by maintaining a minimum systolic blood pressure of 100 mm Hg with a urinary output of at least 50 ml/h. If the patient is being kept dehydrated because of possible cerebral edema, vasopressors may be needed, with dopamine the drug of choice. After brain death is declared, rehydration should be instituted and the patient weaned from vasopressors, if possible. Management of fluids should be directed at matching the previous hour's urinary output plus an additional 100 ml. If diabetes insipidus occurs with urinary output of greater than 500 ml/h for two consecutive hours, small doses of vasopressin should be given to decrease the output. This may diminish the possibility of fatal neurogenic pulmonary edema which can occur before consent can be obtained or brain death declared. All efforts must be taken to prevent infection of the patient to ensure healthy organs for the immunosuppressed recipients. The donor's temperature should be maintained as close to normal as possible, with 35.5°C the minimum for a valid declaration of brain death. All efforts must be made to prevent cardiac arrest.

Initial laboratory investigations should include: blood group, hepatitis B surface antigen, human immunodeficiency virus, renal and hepatic profile, complete blood count, urinalysis, drug screening, and cultures of urine and blood. A chest x-ray study should also be done. These initial tests may reveal information that precludes donation. Serial renal profiles will be needed to adequately manage the donor. If the patient is to be considered for heart donation, cardiac enzyme levels must be determined as well as a 12-lead electrocardiogram obtained. An accurate body weight of the donor should be obtained.

Nationally adopted requirements for a declaration of brain death require that two physicians, one of whom is a neurologist or neurosurgeon, do two clinical evaluations of brain function 24 hours apart and that an electroencephalogram (EEG) be done at the same intervals. Preconditions to the determinations include that an absolute cause for the condition exists; that significant levels of sedatives, narcotics, or depressants are excluded by blood tests; that the patient is not in untreated cardiovascular shock; and that all metabolic or endocrine causes have been excluded. The patient will be maintained on a ventilator and an apneic test performed as part of the testing. The presence of spinal reflexes does not rule out brain death.[1] Both physicians must sign documentation for two separate evaluations and certify that the EEG is isoelectric. If an EEG is unavailable, cerebral angiography may be done to demonstrate the absence of cerebral blood flow.

Difficulties in Organ Donation

Some difficulties have been encountered with the declaration of brain death. The concept of brain death is new to the multicultural medical community in Saudi Arabia and thus there has been some hesitancy to accept findings. This reluctance can also stem from the physician's feelings of failure to save the patient and from the family's strong denial of the potential donor's death. A lack of EEG machines or technicians or required specialists has contributed to delays. If notified promptly, the NKF can either provide the needed equipment or personnel or it can arrange for the patient to be transferred to an institution with the necessary equipment.

Seeking family permission for the removal of organs for transplantation is difficult but necessary. It should be done by a member of the NKF, transplant nephrologist, or their designated member, and preferably by someone of the same nationality. The family should first be informed by the primary physician of the brain death and allowed to absorb this information. Keeping the family informed of the patient's poor prognosis during the entire hospitalization eases acceptance of the final diagnosis. The designated person should then take the family to a quiet place where they can discuss what organs are suitable for transplantation: in Saudi Arabia this includes the kidneys, heart, and liver. The family should be reminded that their loved one is dead; he or she will feel no pain during organ removal; there will be no disfigurement, only a surgical incision; there is no cost or reimbursement for the voluntary donation; the process takes only a few hours and will be arranged as quickly as possible; and that the lives of several people will be enhanced or saved through the donation. If the donor is Moslem, the next of kin should be told or shown records that Islam permits the donation and transplantation process. A special consent form is needed for organ donation. The family may need time to think about this but should be given a time frame in which to make their final decision.

Several factors influence families' decisions. The interval between the initial injury requiring hospitalization until brain death occurs is a major factor. If this period lasts at least two or three days, permission is more likely to be given. The persons present at the time of death including relatives, friends, and professional staff can also influence the family decision. The amount of information given to the family and manner in which it is presented is also important. The education and awareness of the family members about brain death, organ donation, and transplantation greatly influence the decision to donate. The use of donor cards has not yet been effective in the Kingdom, but it is hoped that their eventual use will help to inform the public of organ donation and foster consideration of it among family members before a crisis occurs. The most important factor, however, is the person asking for consent and the manner in which consent is sought. Although one of the most difficult tasks facing any medical professional, it is also one of the most rewarding in that two benefits are reaped. The family of the donor has the assurance that something good has come from their tragic loss and at the same time two or more individuals may have their health restored.

In Saudi Arabia difficulties in obtaining consent have arisen for the expatriate population,[2] which accounts for almost 20% of the population. It may be difficult to locate family members in other countries where there are different time zones, languages, and communication facilities. A relative or co-worker of the potential donor should be a party to the long-distance phone conversation to reassure the family that everything possible has been done for the patient. Often the initial shock of the news is too much and further phone calls are needed. Unlike most Western countries where families can fly to be with their dead family member, expense, time constraints, and visa restrictions largely preclude this option in Saudi Arabia. Phone permission can be obtained if two persons hear the consent, although telex confirmation is preferable. Because of the difficulties associated with expatriate donors, early referral is stressed, with every effort made to locate the family as quickly as possible.

Potential donors can be lost for several reasons, including refusal by the next of kin, inability to locate the donor's relatives, unacceptability of the donor, delayed referral of the donor, or simply no referral. Sometimes donors are not referred because the donation process may be quite involved and entail extra work, or because the attending physicians do not approve of brain death or organ donation. None of these reasons is ultimately acceptable. All possible donors must be referred as soon as brain death is suspected.

After brain death has been confirmed and the family has consented, in the instance of kidney donation, the NKF will contact one of the four transplant centers and arrange for them to fly by Medivac jet to the hospital for kidney retrieval. The patient is pronounced dead before the procedure and maintained on life support systems until the organs are removed. Most teams will bring kidney perfusion and packaging equipment with them. A surgical staff prepared to do a laparotomy is all that is needed. Additional ice may be requested to keep the organs in cold storage. The team will take additional blood, spleen, and lymph node samples to assist with the kidney crossmatch and patient selection. Potential recipients are called from all over the country to be tested.

Current Status of Program

Even considering that the organ donor program is new, donor referrals have been few. Donor referrals to the KFSH&RC increased only slightly from 27 in 1987 to 31 in 1988, though it is encouraging that nine centers in six cities made referrals in 1988. Donors ranged in age from seven months to 55 years. Of those referred to KFSH&RC, road traffic accidents (RTA) were the leading cause of death (45%), followed by brain tumors (24%).

What is encouraging is the success rate in obtaining family consent. In 1987 family consent was obtained for 24% of the donors referred to the KFSH&RC; this improved to 37% in 1988. For the U.S.A., these rates were 10% and 41%, respectively.[3-6] No nationalities should be excluded because of any preconceived idea that certain nationalities will refuse. Most significantly, the increase in success rate of Saudi donation has risen from 11% in 1987 to 37% in 1988. This pays tribute to those who have worked to educate the public about organ donation and transplantation within the Kingdom. It also shows the willingness of the Saudi population to accept organ donation and transplantation, however new the concept, and to help their own people through transplantation.

There is an estimated 55 potential donors per million population, if donor acceptability is limited to ages 5 to 55,[5,7-11] thus placing the donor potential in Saudi Arabia at more than 660 each year. However, only 176 referrals were made to the NKF over a two-year period, with 56 of the families consenting to donation. This means that kidneys were retrieved from only 4.2% of potential donors within the Kingdom, compared to 16.5 to 19.3% in the U.S.A.[5,7,8] With traffic accidents a leading cause of death within the Kingdom and the Riyadh Central Hospital reporting traffic accidents as the major cause of death for patients under age 40,[12] there is a tremendous potential for increasing donor referrals.

If only 33% of the possible 660 donors consented, there would be 220 donors, or 440 kidneys, each year. Nearly 2000 patients within the Kingdom now require replacement dialysis therapy at over 60 dialysis centers, and some one third to one half of them are suitable transplant candidates. If 880 kidneys were obtained over a two-year period, transplantation could be offered to all suitable patients within the Kingdom, virtually eliminating the waiting list.

Transplantation within the Kingdom has been proved successful. According to officials at the NKF, the two-year success rate for cadaveric kidneys is 77%, with 95% patient survival. The one-year success rate for the KFSH&RC first cadaveric recipients is 90%, with 100% patient survival.

Recommendations

Despite some minor difficulties with brain death documentation and obtaining consent from the large expatriate population, all efforts must be concentrated on improving the donor referral system. The responsibility lies with all medical professionals[13] within the Kingdom. Ways of increasing donor referrals include: early referral of any patient with suspected brain death to a transplant center or the NKF, with speedy determination of brain death, keeping the family well informed of the patient's poor prognosis, having consent obtained only by a physician appointed by the NKF, enlisting the help of religious leaders in asking family members for consent, and continually educating both the medical professionals and public about organ donation and transplantation. Donor cards may be an especially simple and effective way to educate the public.

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Appendix A: Senior Ulama Commission's Decision on Organ Donation.

Report of the Senior Religious Leaders Commission's Decision No. 99 dated 6-11-1402H (25-08-1982):

The Board unanimously resolved the permissibility to remove an organ, or part thereof, from a Moslem or Thimmi living person and graft it onto a living person, should the need arise, should there be no risk in the removal and should the success of the transplantation in the recipient seem likely. The Board also resolved, by majority, the following:

A. The permissibility to remove an organ or part thereof from a dead person for the benefit of a Moslem, should the need arise, should the removal cause no dissatisfaction, and should the transplantation seem likely to be successful.

B. The permissibility for the living person to donate one of his organs or a part thereof for the benefit of a Moslem in need thereof.

مضمون قرار هيئة كبار العلماء
رقم ٩٩ وتاريخ ٦/ ١١/ ١٤٠٢هـ

قرر المجلس بالاجماع جواز نقل عضو أو جزئه من إنسان حي مسلم أو ذمي إلى نفسه إذا دعت الحاجة إليه وأمن الخطر في نزعه وغلب على الظن نجاح زرعه كما قرر بالأكثرية ما يلي:

١ـ جواز نقل عضو أو جزئه من إنسان ميت إلى مسلم إذا إضطر إلى ذلك وأمنت الفتنة في نزعه ممن أخذ منه وغلب على الظن نجاح زرعه فيمن سيزرع فيه.

٢ـ جواز تبرع الإنسان الحي بنقل عضو منه أو جزئه إلى مسلم مضطر إلى ذلك وبالله التوفيق وصلى الله على محمد وعلى آله وسلم.

هيئة كبار العلماء

Appendix B: Council of Islamic Jurisprudence Decision on Death.

The Council of Islamic Jurisprudence in its third session held in Amman 13-02-1407 H (16-10-1986 G) discussed the supportive means in intensive care units, and after comprehensive explanation from consultant doctors, decided the following:

A person shall be considered legally dead, and all the legal consequences of death applied, when one of the following signs is confirmed:

A. Complete cessation of the heart or respiration and the consultant physicians decide that the cessation is irreversible.

B. Complete cessation of all functions of the brain and the expert specialist physicians decide the cessation is irreversible, and the brain has started to decompose.

In this condition, it is permissible to discontinue the supportive means from the patient, even though some of his organs, like the heart, still work artificially through the operation of the support system.

القرار رقم (٥) د ٣/ ٧/ ٨٦ بشأن «أجهزة الانعاش»

إن مجلس مجمع الفقه الإسلامي المنعقد في دورة مؤتمره الثالث بعمان عاصمة المملكة الأردنية الهاشمية من ٨ إلى ١٣ صفر ١٤٠٧هـ / ١١ إلى ١٦ أكتوبر ١٩٨٦م.

بعد تداوله في سائر النواحي التي أثيرت حول موضوع «أجهزة الانعاش» واستماعه إلى شرح مستفيض من الأطباء المختصين.

قرر ما يلي:

يعتبر شرعًا أن الشخص قد مات وتترتب جميع الأحكام المقررة شرعًا للوفاة عند ذلك إذا تبينت فيه إحدى العلامتين التاليتين:

١ـ إذا توقف قلبه وتنفسه توقفًا تامًا وحكم الأطباء بأن هذا التوقف لا رجعة فيه.

٢ـ إذا تعطلت جميع وظائف دماغه تعطلاً نهائيًا، وحكم الأطباء الاختصاصيون الخبراء بأن هذا التعطل لا رجعة فيه، وأخذ دماغه في التحلل.

وفي هذه الحالة يسوغ رفع أجهزة الانعاش المركبة على الشخص وان كان بعض الأعضاء كالقلب مثلاً لايزال يعمل آلياً بفعل الأجهزة المركبة.

Case Reports

CHILDHOOD ACHALASIA: REPORT OF THREE CASES

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Achalasia of the esophagus is a neuromuscular disorder that displays a well-known pattern of dysmotility. Besides the loss of primary and secondary peristaltic movements, the lower esophageal sphincter cannot relax.[1] Hydrostatic dilation and/or esophagomyotomy are used to alleviate the problem[2] but results vary. Gastroesophageal reflux can occur and symptomatic relief is not always complete. The natural history of this disorder is difficult to define, as it presents in patients of all ages and the symptoms may not relate to the severity and duration of the pathology.[3] We describe the cases of three children with achalasia and consider relevant points in the diagnosis and management of this rare childhood disorder.[4,5]

Patients and Results

Three children (two infants aged 18 and 17 months and a 14-year-old adolescent—all males) were treated for esophageal achalasia at King Fahd Hospital, Al-Khobar, over a period of 5 years between 1982 and 1987.

The dominant symptoms in both infants were vomiting of undigested food, failure to thrive, and recurrent chest infections that had lasted for 12 and 5 months, respectively. Their growth indices measured below the fifth percentile according to National Centre for Health statistics weight-for-height grids. The adolescent boy presented with heaviness and pain in the chest, progressive dysphagia, nocturnal regurgitations, episodes of chest infection, and weight loss. His symptoms had persisted for 6 years. Family history in all three was unremarkable.

The diagnosis in all was based on clinical history, a wide mediastinum shown by chest x-ray study that also revealed a fluid level in two, and barium studies. The barium studies showed classic dilatation of the esophagus with a tapered lower end (Figure 1) and fluoroscopy revealed weak contractility. There was neither a history nor evidence of reflux on the x-ray study. Esophagoscopy performed in one of the two infants yielded normal findings but showed retention esophagitis in the adolescent.

All three patients underwent a transabdominal modified Heller's esophagomyotomy. One infant also underwent an antireflux procedure. A loose Nissen's fundoplication was also done in the adolescent because the mucosa was inadvertently perforated during the myotomy. The hiatus, which was patulous, was appropriately restored in all three by use of two to three interrupted silk sutures. All three patients recovered rapidly and uneventfully. The children remained asymptomatic during follow-up, which averaged 10 months. They gained weight rapidly and there was no dysphagia or symptoms of reflux. Their recent growth percentiles approached 10.

Discussion

Achalasia is a rare manifestation of esophageal disease in patients younger than 15 years; 70% are 10 years or younger, and infants constitute about 20% of the entire pediatric group.[1] The reports on familial occurrence of achalasia[1,6] are relevant in our patients because of the high incidence of consanguinity in our patient population. Many autosomal diseases prevail in this region; although the observations of local surgical colleagues have not substantiated a hereditary line, it remains a topic that requires further investigation.

Diagnosis is clearcut in cases that exhibit symptoms. Early detection is important in chil-

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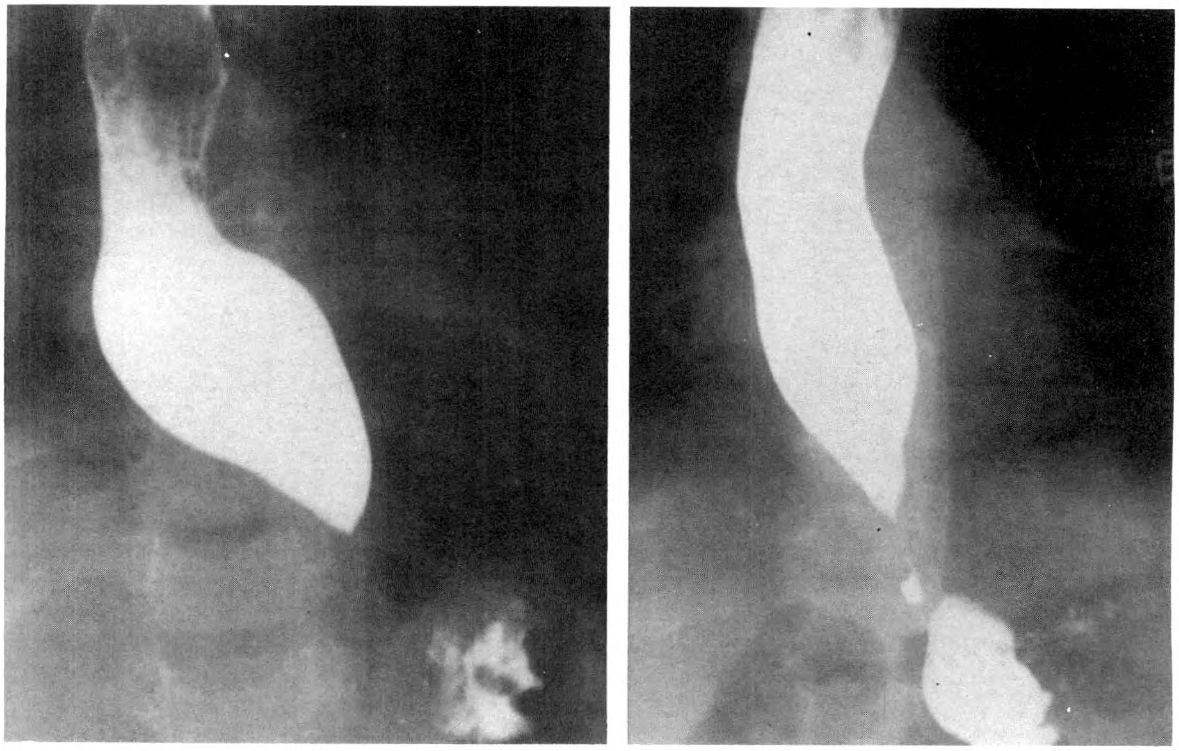

FIGURE 1. Barium swallow showing dilated esophagus with tapered lower end (bird's beak sign).

dren, because of the risks of severe growth retardation and respiratory complications, but the presentation in infants is often atypical.[6,7] It may mimic other disorders of the gastrointestinal tract, in particular gastroesophageal reflux.[7,8] Esophagography, fluoroscopy, and selective esophagoscopy are effective tools in making diagnosis and planning treatment.[3,9] Nuclear (isotope) scan and preoperative and intraoperative manometry have been recommended, if only to rule out the possibility of postmyotomy gastroesophageal reflux.[2]

The treatment of achalasia still engenders controversy. Pneumatic dilatation, which aims to tear the muscle fibers of the lower esophageal sphincter, has been advocated as the initial treatment in adults, and some series show results comparable to those produced by other forms of treatment.[10,11] Dilatation is not advocated as a first-line management in children because of the reported poor results, the high incidence of perforation, and the frequent need for repeated general anesthesia. A modified Heller's myotomy is now the treatment of choice in children with achalasia.[5,6,9] We agree with this view, particularly for a population such as the one we serve in which good follow-up is not always possible, as would be necessary in patients requiring repeated dilatation.

Without good guidelines, the decision to perform an antireflux procedure remains arbitrary.[12,13] Such guidelines are difficult to formulate because of the limited number of cases seen by individual surgeons. Of the many anatomical factors incriminated as the cause of gastroesophageal reflux, our experience suggests patulous hiatus as the most common abnormality.[3]

Over a long time, a progressively enlarging esophagus produces a degree of hiatal incompetence that is revealed when the abdominal part of the esophagus is mobilized during surgery. Because of this, some surgeons recommend a thoracic approach to avoid disturbing the hiatus.[2] An obvious hiatal hernia must be repaired, and in the absence of an obvious hiatal hernia, hiatal competence must also be restored as an essential adjunct to myotomy. Alternatively, a loose fundoplication would serve a similar purpose, besides enhancing the barrier effect of the now attenuated lower esophageal sphincter. It may also be useful for reinforcement in the repair of an inadvertent perforation of the narrow and vulnerable portion of the esophagus just above its junction with the stomach. In children with esophageal achalasia, who are at risk for gastroesophageal reflux, we also recommend some form of loose fundoplication in conjunction with an adequate esophageal myotomy to ensure a satisfactory outcome.

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SUCCESSFUL PREGNANCY IN A PATIENT ON LONG-TERM HEMODIALYSIS

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Successful pregnancy is rare in patients who are on long-term dialysis. We describe normal delivery in a young woman who had been on dialysis treatment for more than four years.

Case Report

A 38-year-old woman with a long history of proteinuria, microscopic hematuria, and hypertension had first been evaluated in September 1983 by the nephrology service immediately after her tenth delivery, which was complicated by postpartum hemorrhage. At that time, she was found to have severe renal failure (serum creatinine, 620 μmol/L) with small kidneys. Renal biopsy was not done. Seven months later, she became progressively uremic and maintenance hemodialysis was commenced on a schedule of four hours three times per week using a 1.3 m^2 hollow-fiber dialyzer and glucose bicarbonate dialysate (sodium, 140; potassium, 2; HCO^3 35 mmol/L). She did well, her interdialytic weight gain averaged 1 to 2 kg, and her serum chemistry levels were acceptable. However, packed red cell transfusions were required every 3 to 4 months to control her anemia. Her residual renal function was 1 ml/min. Her blood pressure remained well controlled throughout this time. There was no clinical or radiological evidence of peripheral neuropathy, renal osteodystrophy, or cardiac dysfunction. Her medications included 1-α hydroxy vitamin D$_3$ supplement (0.5 μg daily) and variable doses of aluminum hydroxide. She had had 10 full-term normal deliveries, the last of which was in September 1983. Her menstrual periods continued to be regular even during dialysis.

In October 1988, the patient felt fetal movements and a 20-week pregnancy was confirmed by ultrasound. Her dialysis regimen was increased to four hours, four times a week with no change in the setting, and more frequent packed red blood cell transfusions were required (Figure 1). Her

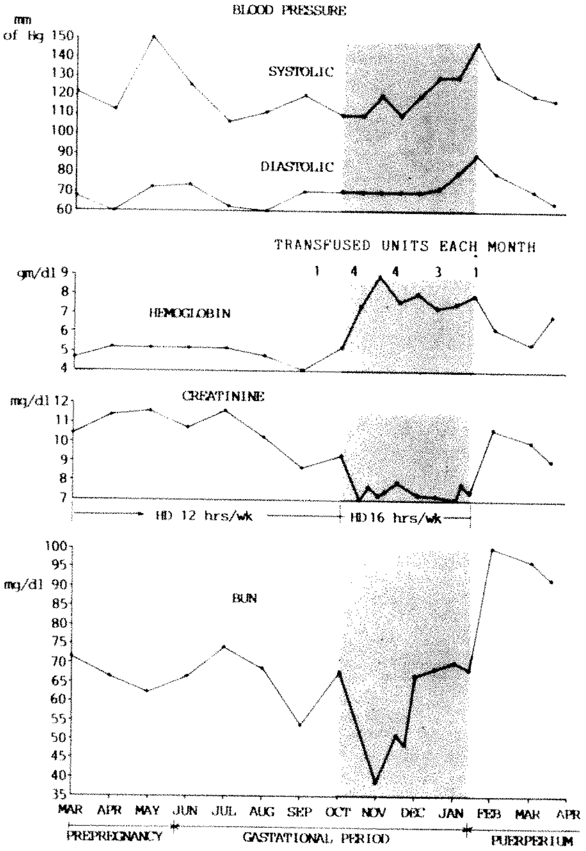

FIGURE 1. Blood pressure control, hemoglobin status, and level of blood urea nitrogen and creatinine in patient before conception and during pregnancy. Shaded areas indicate increased dialysis hours (16 hr/wk) during pregnancy.

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heparin maintenance dose was doubled because of increased clotting of the dialyzers in the third trimester. Her 1-α hydroxy vitamin D_3 dosage was increased to 1 μg daily. Her dialysis sessions during pregnancy were fairly stable and her blood pressure continued to be normal. At 32 weeks of pregnancy, shortly after a hemodialysis session, she experienced labor pains and a 1.9-kg male infant was delivered vaginally without complications. The placenta was macroscopically healthy and weighed 500 gm.

On the third puerperal day, she resumed her usual dialysis regimen (12 hr/week) and the remainder of her puerperium was uneventful. The baby did well and was discharged from the neonatal care unit on the 18th day when his weight was 2020 gm. Although the patient had normal lactation, she did not nurse her baby.

Discussion

Successful pregnancy after long-term dialysis is unusual. Review of the literature revealed that there have been few successful pregnancies in patients on long-term hemodialysis.[1-4] One published review on this subject[5] described patients who had conceived as much as 9 years after they had first started dialysis treatment, but successful pregnancy occurred only in those who had been treated for 4 years or less. An editorial[6] described a patient who had conceived twice after nine years of dialysis, but we could not find the date. To our knowledge, the 4-½ years of maintenance hemodialysis and successful pregnancy seen in our patient represents one of the longest periods reported. Hypertension frequently accompanies chronic renal failure and is often exacerbated by pregancy.[1] Although the clinical value of blood pressure control has not been demonstrated in all case reports, we observed that, overall, normalizing blood pressure was the common denominator in all successful pregnancies.[3] Our patient was always normotensive and we believe this was the main reason for the favorable outcome. In addition, special attention was given to avoid hypotensive episodes during dialysis.

Whether more intensive dialysis treatment is needed in pregnancy is still a controversial issue. Some authors recommend aggressive dialysis to achieve variable target predialysis blood urea nitrogen and creatinine values.[1,3,7] However, our patient received vigorous dialysis only after the 20th week of gestation, by which time organogenesis is completed. This suggests that azotemia may not be the most important factor influencing the outcome of pregnancy. Different authors have suggested different strategies concerning the adequacy of anticoagulation therapy for hemodialysis during pregnancy. Some[8] recommend an increased heparin dosage is necessary to correct the hypercoagulable state of pregnancy while others have reported increased hemorrhagic complications with such an approach.[9] In the present case, doubling of the heparin dose was needed to prevent dialyzer clotting with no resulting adverse effect.

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PERSISTENT MULLERIAN DUCT SYNDROME IN AN ADULT: A CASE REPORT

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Persistent mullerian duct syndrome is a rare form of male pseudohermaphroditism. It is characterized by the presence of well-developed mullerian structures in a male who possesses normally developed external genitalia.[1]

The classic presentation occurs in children and comprises unilateral cryptorchidism and contralateral inguinal hernia that contains the mullerian structures.[2] Recently we encountered the syndrome in a middle-aged man and this influenced the clinical picture as well as management.

Case Report

A 40-year-old Saudi man was first seen at our andrology clinic because of primary infertility. He also complained of erectile dysfunction of 10 years' duration. He had been married for 15 years without producing pregnancy. His past medical history included surgical repair of a right inguinal hernia.

Examination revealed a healthy man with scanty facial hair. There was no gynecomastia, but his pubic hair was somewhat feminine in distribution. The phallus was normal but the scrotum was empty and underdeveloped. No testicles could be palpated in either inguinal region. There was a right inguinal scar remaining from the hernia repair. Rectal findings were unremarkable.

A spermogram on three occasions revealed azoospermia, and the semen was positive for fructose. The serum testosterone level was less than 1 nmol/L (reference interval, 10.4-31); luteinizing hormone, 40 IU/L (reference interval, 3-18); and follicle stimulating hormone, 80 IU/L (reference interval, 3-16). Pelvic ultrasound examination showed a solid mass on the right side. The left testicle was not identifiable. Computed tomogram showed a 6 × 4 × 3 cm soft tissue mass in the right paravesical region that projected posterior to the urinary bladder and could not be differentiated from the right seminal vesicle (Figure 1). The radiological diagnosis was undescended testis, with malignant transformation.

On surgical exploration through a lower abdominal incision, the left testis was found to be soft, small, and grossly dysplastic. The epididymis was cystic and separated from the testis. Attached to the epididymis was a mass that extended from the left internal inguinal ring to the right one and descended behind the bladder (Figure 2). The gross appearance was that of the broad ligament and uterus. It was excised and found to consist of a uterus, cervix and vagina, broad ligament, two

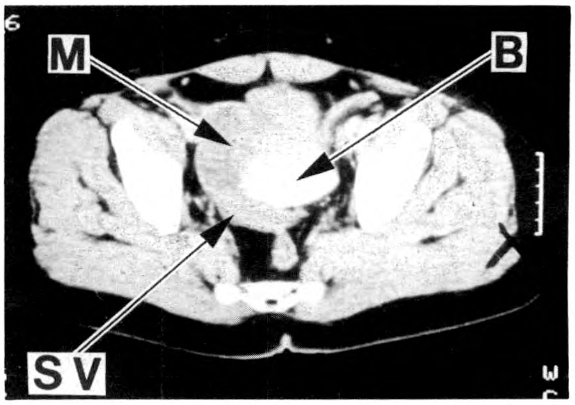

FIGURE 1. Computed tomogram of the pelvis showing the urinary bladder (B), the seminal vesicles (SV), and the mass (M).

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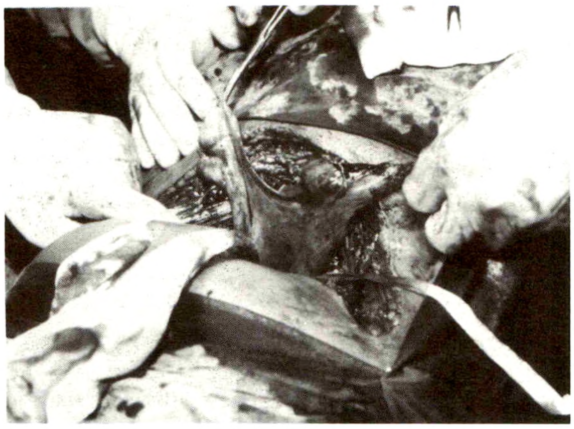

FIGURE 2. Operative photograph showing the pelvic mass before resection.

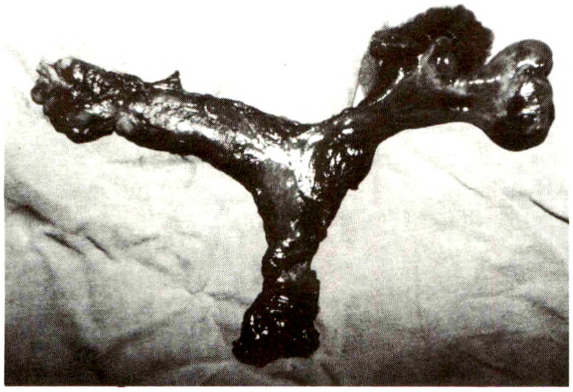

FIGURE 3. Gross appearance of the resected specimen with the dysplastic left testicle.

fallopian tubes, and a dysplastic left testicle (Figure 3). No testicle was found on the right side. Subsequent buccal smear was chromatin-negative. Postoperatively he was started on testosterone replacement therapy.

Discussion

Through the effect of the H-Y antigen on the Y chromosome, the developing testis produces testosterone and mullerian inhibitory factor. Testosterone induces the virilization of the ipsilateral wolffian duct. Virilization of the external genitalia is influenced by dihydrotestosterone, which represents the reduced active form of testosterone produced intracellularly by alpha$_5$-reductase.[3,4]

Mullerian inhibitory factor is a poorly characterized polypeptide hormone secreted by the fetal Sertoli cells that acts locally on the ipsilateral side of the testis and leads to retrogression of the mullerian ducts.[5,6] In its absence, as in normal females, the mullerian ducts give rise to the uterus, fallopian tubes, and the upper third of the vagina.

Persistent mullerian duct syndrome is an inherited condition, and it is probably inherited as an X-linked recessive or a male sex-limited autosomal trait.[1,7,8] One theory for persistent mullerian duct syndrome is that it results from failure of production, release, or lack of response of the target organs to mullerian inhibitory factor.[7]

Typically the syndrome is seen in children and presents as an inguinal hernia, with or without a contralateral undescended testis. The hernial sac contains the mullerian structures.[2] Our patient, who was 40, presented with testicular failure (i.e., impotence, infertility, poorly developed secondary sexual characteristics, and the hormonal pattern of hypergonadotrophic hypogonadism).

The associated cryptorchidism in our patient could be due to lack of mullerian inhibitory factor. Donohoe[9] suggested that this factor plays a role in normal testicular descent. However, cryptorchidism is most likely due to mechanical interference in the normal testicular descent by the mullerian structures.[10,11]

Isolated persistent mullerian ducts must be differentiated from gonadal dysgenesis. In both instances there are mullerian structures; however, in the former the external genitalia are normal while in the latter they are ambiguous. It is important to make this distinction because gonadoblastomas were found in 40% of the cases of gonadal dysgenesis reported by Josso et al.[11] Sex assignment in patients with persistent mullerian duct syndrome is obvious because all show a male phenotype.

Primary orchidopexy should be done in affected children. However, because the vas deferens is closely associated with the broad ligament, removal of the mullerian structures should be avoided to prevent injury to the male genital ductal system if fertility is to be maintained.[8,10] However, because of our patient's age, the obvious anomalies of the epididymis, and the endocrinal picture of primary testicular failure, his mullerian duct structures were removed.

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GLANZMANN'S THROMBASTHENIA TYPE II IN A SAUDI CHILD: A CASE REPORT

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Glanzmann's thrombasthenia is a rare intrinsic platelet disorder characterized by a lifelong bleeding tendency with normal coagulation profile, normal platelet count, reduced or absent clot retraction, prolonged bleeding time, and absent platelet aggregation to adrenaline, adenosine diphosphate, and arachidonic acid. There is also markedly reduced or absent collagen aggregation while ristocetin produces either irreversible aggregation or aggregation followed by disaggregation.[1] This disorder is associated with the selective absence or abnormalities of platelet glycoproteins IIb and IIIa.[2] Although Glanzmann's thrombasthenia is rare in the Western world,[3] it is somewhat more common in developing countries.[4] A few cases have been reported in Iraqi Jews[5] and Jordanian Arabs.[6] We present what we believe is the first case of Glanzmann's thrombasthenia type II reported from Saudi Arabia.

Case Report

A 2-year-old Saudi boy was first seen at King Khalid University Hospital in May 1987 because of continuous and spontaneous nose bleeding and ecchymoses on the day of admission. He had been born full term by a normal home delivery. At one month of age he bled profusely after circumcision, and at 8 months, he bled from one site of dental eruption. Ecchymoses were observed to form after minor trauma but there were no joint swellings. His parents are first degree cousins. His mother had a spontaneous abortion at 5 months in her third pregnancy.

On physical examination the patient was found to be mildly pale and bleeding from both nostrils. There were no petechiae on the skin or mucous membranes. There were multiple ecchymotic spots on the upper and lower extremities. General physical as well as neurological findings, including fundi, were normal. Bleeding from nostrils was stopped by packing and neither platelet nor blood transfusion was necessary.

To evaluate the disorder, blood from the child and his parents was collected for standard hemostatic tests.[7-9] Platelet glycoprotein was obtained in 3.8% trisodium citrate (1 part to 9 parts blood) and tested using the method of Newman et al.[10]

A murine monoclonal antibody, designated AP-3, that was specific for the glycoprotein IIIa/IIb complex had been prepared by immunization with glycoprotein IIIa-enriched and glycoprotein IIb-enriched triton X-114 extract of platelet membranes. It has been shown that glycoproteins IIb and IIIa are complexed in a 1:1 stoichiometry in the plasma membrane of intact nonactivated platelets.[10] The murine monoclonal antibody reacted solely with glycoprotein IIIa derived from the patient's blood. The epitope on glycoprotein IIIa recognized by AP-3 is expressed on dissociated glycoprotein IIIa as well as on calcium-dependent complexes of glycoproteins IIb and IIIa by crossed immunoelectrophoresis.[10]

The results of the patient's coagulation screening tests are shown in Table 1. The platelet aggregation fulfilled the diagnostic criteria for Glanzmann's thrombasthenia type II (Figures 1, 2). The results of both parents' coagulation tests were within normal limits, with intermediate values for the glycoprotein IIb/IIIa complex.

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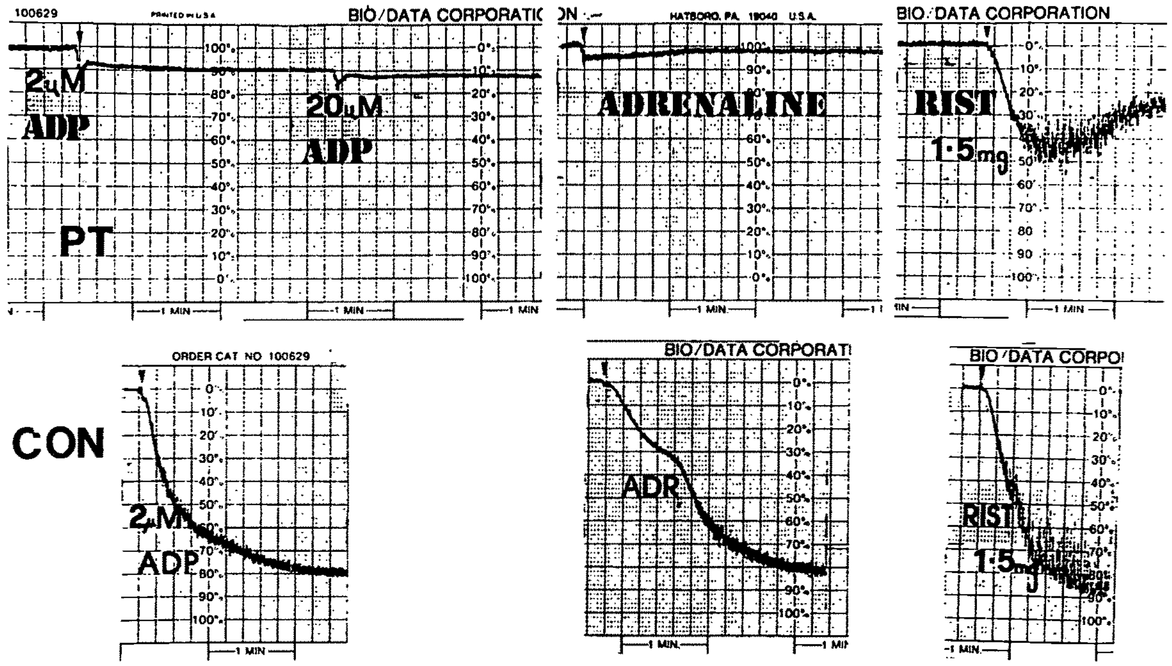

FIGURE 1. Response curves of platelets of patient (PT) and control (Con) to adenosine diphosphate (2 μM and 20 μM), adrenaline, and ristocetin (Rist, 1.5 mg).

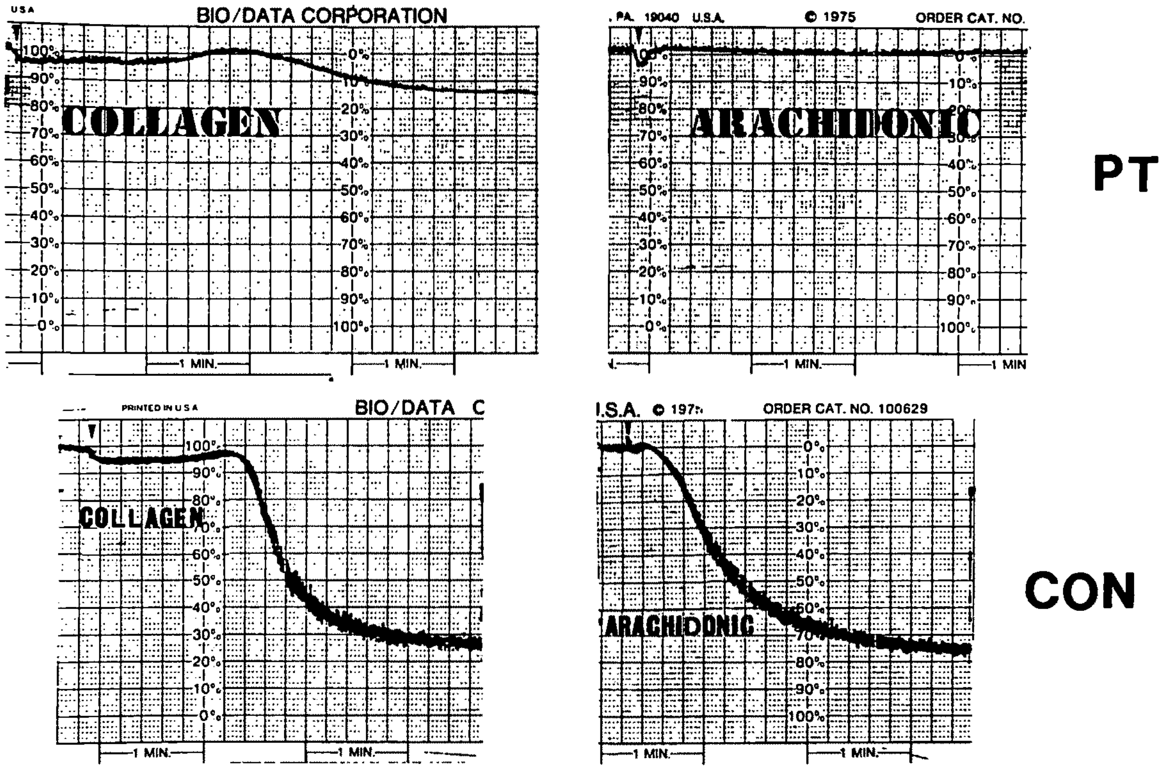

FIGURE 2. Curves showing lack of response of platelets of patient (PT) to arachidonic acid and a reduced response to a collagen stimulus as compared to that of control (con).

TABLE 1. *Results of hemostatic function tests.*

Hemostatic test and platelet glycoproteins	Patient values	Normal values
Bleeding time (min) (Duke)	13	2–4
Platelet count ($\times 10^9$/L)	450	150–450
Prothrombin time (sec)	11.6	10.9
Partial thromboplastin time (sec)	26.2	27.4
Fibrinogen (g/L)	4.87	1.5–4.0
Thrombin time (sec)	18.8	16.2
Reptilase time (sec)	12.2	12.6
Antithrombin III (%)	108	80–120
Factor VIII:C (%)	250	52–188
Hess test	strongly positive	
Clot retraction	0	
Glycoproteins/platelets		
GPIIIa/IIb complex*	10,000	≥40,000

*GPIIIa/IIb is 18,700/platelet and 21,000/platelet for the mother and father, respectively.

Discussion

The findings in our patient (Table 1) indicated a qualitative platelet disorder and established the diagnosis of Glanzmann's thrombasthenia type II.[1,2] Glanzmann's thrombasthenia has an autosomal recessive pattern of inheritance with both sexes affected equally. At least two types of the disorder have been recognized and are termed type I and II depending on the absence or abnormalities of platelet glycoproteins IIb and IIIa.[2] In type I, glycoproteins IIa and IIIb are absent, and therefore platelets do not bind fibrinogen. In type II, the platelets are reduced to 10 to 20% of normal[11] and are capable of binding subnormal amounts of fibrinogen.[12,13] The platelets also fail to aggregate in response to various aggregating agents. Conversely, thrombasthenic platelets exhibit the unique feature of aggregation followed by a disaggregation in response to high doses of ristocetin.[14] Reversible ristocetin aggregation is not a common accompaniment of other bleeding disorders.[15] Patients with type I disease are usually severely affected; those with the type II or heterozygotes form[16] may have mild or no symptoms.

Although Caen[17] stressed the amelioration of bleeding manifestations with age, Reichert et al[5] have confirmed that bleeding manifestations persist into adulthood. Some patients benefit from allogenic bone marrow transplantation,[18] but in many platelet transfusion therapy controls the bleeding or epistaxis.[1]

Acknowledgment

I would like to thank Ms. Vergie Vicente for secretarial assistance.

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Letters to the Editor

The *Annals of Saudi Medicine* welcomes letters to the Editor from its readers. They may be on any topic, though the Editor especially encourages discussion of papers published in the *Annals*. Letters should be no more than 100 typewritten lines in length, typed double-spaced, and submitted in triplicate. Letters may include one figure or brief table and up to five references. Submission of a letter constitutes permission for the *Annals* to use it for publication, and letters should not duplicate similar material being submitted or published elsewhere, and the *Annals* reserves the right to edit letters submitted. Letters referring to a recent *Annals* article should be received within 6 weeks of the article's publication.

Behcet's Disease in Saudi Arabia

To the Editor: The article on Behcet's disease by Al-Dalaan et al[1] was a nice review and made excellent reading. However, a few points need to be mentioned.

Superficial and deep vein thrombosis is seen in one fourth of all affected patients. Pulmonary embolism, however, appears to be a very rare complication. Familial occurrence has been reported, and in patients from the Mediterranean area and Japan, the disease appears to be linked to HLA-B5 and HLA-DR5 autoantigens.[2]

Bizarre forms of arterial and venous thrombosis or arterial aneurysm formations should suggest Behcet's disease as a possible diagnosis. Cardiovascular involvement occurs in 7 to 29% of cases, and up to 20% of those patients with prominent vascular involvement die of this complication. Venous lesions, ranging from recurrent superficial thrombophlebitis to occlusion of the superior and inferior vena cavae, are more common than the formation of arterial occlusions or arterial aneurysms, which account for most of the deaths from vascular causes. Most interesting is the propensity for arterial aneurysms to form after arterial puncture in patients with Behcet's disease.[3]

Thrombosis of the major veins is twice as common as arterial involvement, occurring in order of frequency in the superior vena cava, inferior vena cava, femoral, subclavian, common iliac, hepatic, and greater saphenous veins. Renal involvement, which was previously considered rare, is now seen more frequently.

Madkour and Kudwah[4] believe that the pattern of Behcet's disease in Saudis is unusual because of the strong evidence of an infective etiology and of the disease's susceptibility to hormonal influence. In their study of two unrelated families, they found that in the first family the father was initially affected, and one year after marriage his wife, who was unrelated and previously healthy, developed the disease. Pregnancy caused severe and prolonged exacerbations of her arthritis and ulcers; only at menopause did she become free of all symptoms. She had ten children; Behcet's developed in eight (six females, two males), and occurred after puberty in all. After the marriage of two of her daughters, the respective husbands began to exhibit symptoms of the disease approximately one year after marriage. Both husbands had been previously healthy. Neither marriage was consanguineous, and both women noticed that their symptoms were aggravated by the contraceptive pill and pregnancy. In the second family, the disease occurred in a woman five years after marriage to a man with acute Behcet's disease. Pregnancy also exacerbated her symptoms.

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Renal Involvement in Behcet's Disease

To the Editor: Behcet's disease is a multisystem disorder whose main clinical features include recurrent aphthous stomatitis, recurrent genital ulceration, uveoretinitis, and skin vasculitis. Almost every form of systemic involvement has been described, especially central nervous system disease, arthritis, venoarterial occlusion disease, inflammatory bowel disease, and pleuropulmonary disease.[1]

Despite the systemic nature of Behcet's disease, only isolated case reports and a few studies have documented significant glomerular involvement. This can take the form of renal amyloidosis, glomerulonephritis, or glomerular deposits of immunoglobulins and complement.

In a study of 46 patients with Behcet's disease in Saudi Arabia,[2] only one patient showed renal involvement, manifested by hematuria and proteinuria. Mesangial proliferative glomerulonephritis was seen on a renal biopsy specimen.

We are conducting a prospective study of kidney involvement in Behcet's disease.[3] In this ongoing study, needle kidney biopsy specimens were obtained from 19 patients with Behcet's disease. Seventeen had proteinuria (24-hour urine protein, > 300 mg) and two had microscopic hematuria. There were 14 males and five females, and mean age was 28.6 years (range, 13-39). Mean duration of the disease was five years (range, 1-12). Eighteen patients met O'Duffy diagnostic criteria for complete disease.

Thirteen biopsy specimens were studied by both light and electron microscopy: three had normal glomeruli and ten had variable degrees of mesangial glomerulopathy (mesangial widening and/or hypercellularity). Discrete mesangial electron-dense deposits were seen in three cases. Glomerular sclerosis was encountered in two cases. Five cases were studied by light microscopy alone, four of which had appreciable mesangial glomerulopathy. Immunofluoresence microscopy was done in 17 cases, and glomerular IgA deposits were observed in ten. IgA was the dominant immunoglobulin deposit in seven. There was no correlation between the degree of renal pathology and the glomerular filtration rate, 24-hour urine protein concentration, disease severity, or specific organ involvement except for a positive association with erythema nodosum ($P < 0.02$).

We have also encountered a case of renal amyloidosis that was associated with Behcet's syndrome.[4] The patient was first seen in 1979; he returned in 1982 with chronic renal failure and died in the hospital.

The study of Al-Dalaan et al sheds more light on this disease in the Middle East. It is usually treated by dermatologists, ophthalmologists, or general practitioners who focus on the primary clinical presentations and not the possible serious involvement of other organs or systems, particularly in the initial phase.

According to our study, mesangial glomerulopathy and glomerular IgA deposits occur frequently in Behcet's disease. Further studies are needed to determine the course and significance of such involvement. We recommend a renal function work-up on all patients with Behcet's disease to exclude the possibility of glomerulopathy or amyloidosis, as especially the latter can prove fatal.

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T-cell Lymphomas and HTLV-1 Infection as Observed in Saudi Arabia

To the Editor: In a recent issue of the *Annals*, Ali et al[1] describe their experience with cases of malignant lymphomas seen at the King Faisal Specialist Hospital and Research Centre, Riyadh. Staining by the avidin-biotin complex technique on unfixed fresh tissues obtained from patients with non-Hodgkin's lymphomas was done using a panel of different T- and B-lymphocyte surface antigens.[1] This has revealed that, of the 211 large cell lymphomas discovered in Saudi adults, 37.3% were T-cell type. Categorization of lymphocytes into the two types was not feasible in unidentified lymphomas from Saudi patients because the biopsies had been performed elsewhere and unfixed tissues for snap-freezing were not available.[1] Nevertheless, an immunological classification of lymphocytes in lymphoid tissue fixed in formalin and embedded in paraffin could always be attempted with the avidin-biotin complex staining using the monoclonal antibody preparation L26. This preparation is an unclustered pan-B cell reagent and identifies all B cells, even in routinely fixed and embedded tissues. Except for B cells in cases of acute lymphoblastic leukemia, L26 is a specific marker for B-cell differentiation in non-Hodgkin's lymphomas. It also has a sensitivity and specificity comparable to other B-cell-related marker reagents.

Staining with L26 on 40 B-cell lymphomas was uniformly strong in 37 cases except for two cases of malignant plasmocytic lymphoma and one case of common acute lymphoblastic leukemia. Moreover, staining of 18 T-cell lymphomas with L26 was not successful except in one instance.[2] L26 for use in staining malignant lymphomas would be desirable to assess the national frequency of T- and B-cell lymphomas in Saudi Arabia. Its application would ensure that the reported mean, 37.3%,[1] and the 95% confidence interval of 30.8 to 43.8% observed for T-cell lymphomas in the Riyadh population were representative of their overall incidence in Saudi Arabia.

No details are available regarding re-confirmation of the initial positivity for HTLV-1 antibody in seven of the 130 patients with malignant lymphomas.[1] False-positive results from the retrovirus antibody screen in antiglobulin-based enzyme linked immunosorbent assay (ELISA) tests have led to insurmountable problems. The possibility of a false-positive has to be eliminated by repeated testing using a different ELISA test system, as well as by confirming all repeated ELISA positives with an immunoblot test (Western blot) or radioimmunoprecipitation (RIPA) testing. In a recent multicenter HTLV-1 antibody screening program carried out in Australia on 9642 prospective blood donors, only 20 donors were repeatedly reactive using an Abbott or Dupont ELISA test system.[3] Of the 20 samples in which the Dupont test was used, 18 were nonreactive in the Abbott test system, 17 produced an indeterminate Western blot pattern, and one was negative on the Western blot. The two samples that were reactive in both of the ELISA tests produced an indeterminate result on the Western blot. Definite evidence of anti-p24 reactivity was observed only in two samples. An HTLV-1 antibody screen conducted by the American Red Cross also showed that samples lacking anti-p24 reactivity on immunoblotting were unlikely to be positive on RIPA. Furthermore, the authors do not indicate whether screening for HTLV-1 antibody was done in age-matched and sex-matched patients with other malignancies who were seen at the hospital.

Undoubtedly extensive studies would be necessary to determine the seroprevalence of HTLV-1 antibody in different regions of Saudi Arabia.[1] Such large population surveys for HTLV-1 antibody could also be accomplished by testing pooled serum samples. Pooling of individual serum samples has been technically feasible for detecting HIV-1 in 1380 American patients seen at a sexually transmitted diseases clinic and 1380 health care workers in a hospital in Africa. ELISA testing with pooled sera is not only cost effective but also a highly sensitive and specific way of estimating the extent of HIV-1 infection in a large population.[4] Pooling of sera merits evaluation in Saudi Arabia.

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Reply

To the Editor: We agree with Dr. Arya and his colleagues about the need for assessing the frequency of T- and B-cell lymphomas in the Kingdom of Saudi Arabia. Although immunological classification could be attempted in lymphoid tissue fixed in formalin and embedded in paraffin, the results are usually erratic. Consequently, most reputable laboratories prefer to rely on the avidin-biotin complex technique on unfixed frozen tissue, as we did. Furthermore, as there was no bias in patient selection, the results obtained in our studies may still be considered representative of the overall lymphoma pattern in Saudi Arabia. Regarding the positivity of HTLV-1 antibodies in seven of 130 patients with malignant lymphoma, the test used was the antiglobulin-based ELISA technique. Admittedly, the test is subject to higher false positivity compared to the Western blot or RIPA technique. However, the results obtained indicate that elevated HTLV-1 antibody titers in patients with malignant lymphoma are relatively uncommon in Saudi Arabia. The prevalence of the HTLV-1 carrier state in Saudi Arabia and its possible role in the causation of lymphoma is the focus of studies currently being conducted at this institution. A follow-up report may be available in the near future.

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The Pattern of Brain and Spinal Cord Tumors in the State of Bahrain

To the Editor: I read with interest the study of Dr. Jamjoom[1] on the pattern of intracranial space-occupying lesions in Saudi Arabia and Dr. Amr's comparative data on intracranial neoplasms in Egypt, Jordan, and Syria.[2] I would like to provide additional data from Bahrain on the pattern of brain and spinal cord tumors diagnosed histologically from operative biopsy specimens during the years 1952 through 1986. During this period there were 2524 Bahraini patients with malignant neoplasms, of whom only seven (0.3%) had brain and spinal cord tumors. There was only one patient with a benign neoplasm of the spinal cord and none with benign brain tumor. Because postmortem examination in Bahrain is limited only to medicolegal cases, routine autopsies were not possible in our series.

Of the eight patients, five had spinal cord tumors (benign intramedullary neurilemoma, myxopapillary ependymoma of borderline malignancy, malignant meningioma, malignant glioma, and metastatic deposit of adenocarcinoma), and three had brain tumors (neuroblastoma, malignant astrocytoma, and non-Hodgkin's lymphoma).

Although the global incidence of brain and spinal cord neoplasms is low, the very low incidence of these tumors in Bahrain compared to that of Iraq[3] and Saudi Arabia[4] can be attributed to two main factors—population size and the registration of the tumors. Bahrain is a small country with a population of 238,420, according to the last census of 1981. A low incidence would be expected for such a small population. On the other hand, since specialized neurosurgical units are not available in Bahrain, the majority of local patients with space-occupying lesions of the central nervous system are referred to overseas centers for histological diagnosis and therapy, and these patients therefore escape local registration in Bahrain. All the cases reported here were diagnosed histologically in Bahrain. Our findings point up the need for establishing a local cancer registry for cases diagnosed in Bahrain as well as elsewhere.

None of the patients in Jamjoom's study had lymphoma, although it is the most common primary cancer in Saudi Arabia.[1,2] Lymphoma is also the most common malignant neoplasm in Bahrain[5] and one of our cases, a 60-year-old Bahraini patient, had cerebral non-Hodgkin's lymphoma.

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Hamartoma or Mesenchymoma?

To the Editor: We are very interested in the chest wall hamartoma in an adult reported by Harding et al,[1] and indeed recognize it as the lesion more commonly encountered in the lung, except that the clefts are lined by mesothelium rather than epithelium. The authors' definition of hamartoma is accurate and following from this it is perhaps reasonable for them to assume that their 44-year-old patient had harbored the lesion "for many years, probably since birth." However, as evidenced by the age incidence of the pulmonary lesions, this assumption is probably wrong. In a series of 154 patients with such pulmonary tumors, the peak incidence was in the sixth decade, with only three patients less than 20 years of age.[2] Furthermore, sequential radiographs showed that in 55 patients the tumor first appeared in adult life, and that in 53 it progressively increased in size. The age incidence and progressive growth led us to conclude that the pulmonary tumors were benign neoplasms, rather than hamartomas. This is probably also true of the chest wall tumor reported by Harding et al. We consider the clefts inclusions rather than an integral component of the neoplasm, and suggest that the name *mesenchymoma* is more appropriate to a benign neoplasm composed of diverse connective tissue.[2]

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This letter was referred to two of the senior authors of the original article, one of whom offered the following comment:

Chest wall hamartomas are exceptionally rare even if we call them mesenchymomas. In over thirty years of thoracic surgery and something over 12,000 cases, I have not seen a chest wall hamartoma. In reviewing the Mayo Clinic experience since 1960 and the University of Virginia experience since 1956, we found no recorded cases of chest wall hamartoma. The comments of Doctors Corrin and Wagenaar are very much appreciated.

Editor's Note: Hamartomas are tumor-like congenital malformations made up of tissues normal to the part in which they arise. These tumors usually stop growing when the person stops growing, and are arranged in an irregular, haphazard way. They were first described by Albrecht[1] in 1904. They are not true tumors and differ from teratomas, which are made up of multiple tissues *foreign* to the part in which they arise—heterotopia. Examples of hamartomas more common than the chest wall lesion discussed in the preceding correspondence include solitary exostosis (osteochondroma), and liver and kidney hamartomas. The main point made by Wagenaar and Corrin concerns the presentation of these lesions relatively late in life, after the person has stopped growing, hence their preference for the term "mesenchymoma."

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Need for a Spinal Injuries Center in Saudi Arabia

To the Editor: In the last two decades Saudi Arabia has achieved miracles, not only in areas such as industry, housing, and roads, but also in its medical service. Cardiac and renal transplantation, in vitro fertilization, and other highly specialized medical and surgical procedures are carried out routinely. This rapid transformation has brought with it unforeseen problems–one is paraplegia due to spinal fractures. The cause of spinal fracture is usually trauma, whether a motor vehicle or industrial accident. Road traffic accidents are the second major medical problem in Saudi Arabia.[1] It is estimated that, in the United States alone, 32 patients are admitted per million per year with spinal fractures and of these half remain permanently paralyzed.[2] The condition of 25% of these patients worsens temporarily or permanently due to poor transport, improper immobilization, and poor diagnosis. A study conducted by the World Health Organization concluded that the final disability can be reduced by 50% if the injury is precisely diagnosed.[3]

At present there are no statistics for spinal fractures in the Kingdom. At the King Fahd University Hospital, Al-Khobar, records indicate that, between 1982 and 1988, 101 patients were admitted with thoracolumbar spinal fractures with and without paraplegia.[6] Many other hospitals in the Eastern Province (i.e., Ministry of Health and private), including the trauma centre at Al-Hassa, also treat these fractures. These injuries may be more common here than in the United States.

Every effort is being made by governments, news media, traffic police, and industrial safety committees to prevent accidents by educating the work force and the public to proper safety measures. Despite all this, accidents still occur that lead to spinal fractures.

The benefits of managing patients with spinal fractures at spinal centers are well documented.[4,5] The trained personnel of the spinal injuries center work as a team comprising orthopedic surgeons, neurosurgeons, urologists, nurses, physiotherapists, and occupational therapists. They not only care for the acutely injured patient in a medical sense, but also help the paraplegic adjust to his or her physical incapacity and their life at home and in the community. This can be best achieved in the Kingdom through the services of a spinal injuries center.

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Intravenous Gammaglobulin Therapy for Children with Idiopathic Thrombocytopenic Purpura

To the Editor: We report our experience with high-dose intravenous gammaglobulin (IVGG) therapy in a group of children with both acute and chronic idiopathic thrombocytopenic purpura (ITP) seen in a general hospital in Kuwait.

Twelve children, five with acute and seven with chronic ITP, were studied. The diagnosis of ITP was based on the presence of thrombocytopenia (platelet count, < 50 × 10^9/L). Bone marrow aspiration was used to screen for hematological malignancy, infiltration, and aplasia. Other causes of thrombocytopenia such as systemic lupus erythematosus were ruled out by appropriate tests. Acute ITP was defined as sudden onset of thrombocytopenia with complete cure within six months of onset, and chronic ITP was defined as thrombocytopenia with insidious onset that had lasted for at least six months.[1,2] After the observation period, patients were identified retrospectively as having either acute or chronic ITP.

Treatment consisted of daily intravenous infusion of immunoglobulin, 400 mg/kg of body weight (Intraglobin; Biotest Pharma, West Germany) for five consecutive days. Intraglobin is a human immunoglobulin containing more than 90% IgG. Platelet count was monitored during therapy and in the follow-up period. An increase in the platelet count to at least 100 × 10^9/L following treatment was considered a good response to therapy. Transient response was defined as an initial increase in the platelet count to 100 × 10^9/L that eventually decreased below that level. Maintenance of a platelet count of 100 × 10^9/L during the observation period was regarded as a permanent response. Patients were followed for a minimum of one year.

Four of the patients with acute ITP responded to IVGG and showed an increase in the platelet count to more than 100 × 10^9/L (80%) on the fifth day of therapy (Table 1); three achieved permanent remission with a single course of IVGG. The thrombocytopenia in Patient 4 was associated with the onset of Guillain-Barre syndrome. Spontaneous remission occurred two months later and this coincided with improved muscle function. Five children with chronic ITP responded initially to IVGG treatment but only one (Patient 8) achieved permanent remission. The response was transient in the remaining patients with relapse within 2 to 4 weeks after IVGG therapy. All children with chronic ITP except one were younger than 5 years at presentation.

TABLE 1. *Summary of patient data.**

Patient no.	(y)	Pretreatment/ posttreatment platelet count (100 × 10^9/L)	Outcome
1	2	11/451	Relapse after 1 month, spontaneous remission after 2 months
2	2.5	5/174	Permanent response
3	6	17/323	Permanent response
4†	8	20/NR	Spontaneous remission 2 months later with improvement of muscle function
5	8	10/288	Permanent remission
6	2	13/306	Transient response (2 w)
7	2.5	5/133	Transient response (4 w)
8	3.5	16/228	Permanent response
9	4	14/NR	Mild thrombocytopenia and minor bleeding
10	4	18/NR	Successful splenectomy 2 years later
11	4	14/153	Transient response (2 w)
12	9	14/293	Transient response (4 w)

*Patients 1 to 5: acute idiopathic thrombocytopenic purpura; Patients 6 to 12: chronic idiopathic thrombocytopenic purpura.
†Patient with Guillain-Barre syndrome.
NR = no response.

Our findings demonstrate that the initial response to high-dose IVGG was comparable for both the acute and chronic forms of ITP (80% versus 71%, respectively). However, permanent remission was higher in those patients with acute ITP (60% versus 14%). This has also been observed by others.[3,4] The primary aim of IVGG in children with ITP is to achieve a rapid and significant increase in the platelet count to prevent serious internal bleeding in those with severe thrombocytopenia. This was achieved in 75% of our patients within five days of therapy. Serious side effects to this therapy developed in none of our patients, though low-grade fever and skin rash developed in two children. However, there are reports of adverse effects such as the transmission of non-A, non-B hepatitis.[5]

High-dose IVGG therapy should be considered in any child with ITP who needs a rapid rise in their platelet count, particularly after head trauma or prior to surgery. It is also important in children younger than 5 years of age who have chronic ITP so that splenectomy can be postponed or even prevented.

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Filarial Chyluria

To the Editor: Chyluria results from obstruction and rupture of the lymphatics draining the urinary bladder or pelvis of the kidney.[1] A common cause of chyluria is *Wuchereria bancrofti* filariasis in endemic areas.[2,3] Other possible causes include retroperitoneal tumors, pregnancy, trauma, and surgery. We report a case of chyluria caused by *W. bancrofti* filariasis.

The patient was a 22-year-old Indian man who had arrived recently in Saudi Arabia for the first time. A few months after his arrival, chyluria developed for which he sought medical advice in many district health centers. The chyluria subsequently disappeared spontaneously but recurred after several weeks. He was referred to the King Faisal Hospital in Taif because of an apparently persistent urinary tract infection.

The patient described no symptoms apart from color changes of his urine. He had had no symptoms over the previous two years. Clinical examination showed no abnormalities. Total white blood cell count was 10,000/mm^3 with 15% eosinophils. Urine was creamy white and contained cholesterol, triglycerides, and protein. Lymphangiography revealed dilated lymphatic vessels draining the renal system, mainly the left kidney (Figure 1). Giemsa-stained films of venous blood taken at 12 midnight showed typical *W. bancrofti* microfilariae. The pathognomonic feature of these microfilariae, i.e., the nuclear material did not extend into the tip of the tail, was clearly ascertained. The patient was started on diethylcarbamazine tablets, 50 mg daily, for one week and the dosage increased to 150 mg daily for five weeks. The chyluria disappeared completely within three months with no recurrence during one year of follow-up.

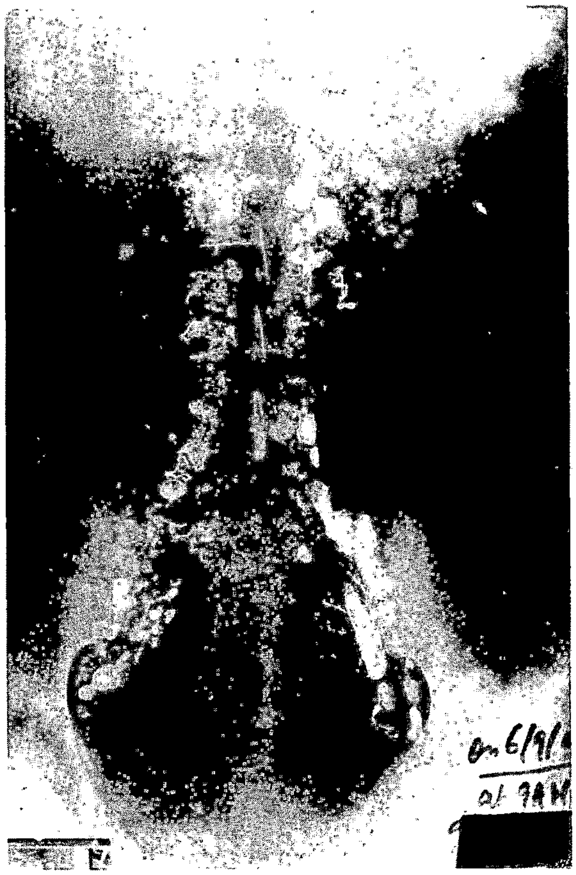

FIGURE 1. Lymphangiogram showing dilated lymphatic vessels draining the renal system, mainly the left kidney.

In 1973, 23 cases of *W. bancrofti* filariasis were reported by the Central Laboratory in Riyadh.[4] During 1973 and 1974, two cases were detected in expatriates living in Makkah and Taif, and there were three cases in Saudi citizens who had not traveled outside the country.[5] Our case is clearly imported *W. bancrofti* filariasis, complicated by chyluria. We think that regular screening programs for bancrofti filariasis in southwestern Saudi Arabia are advisable. Our experience also shows that color changes in the urine is a useful diagnostic clue and inspection should be done personally by the treating physician.

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Successful Treatment of Acquired Amegakaryocytic Thrombocytopenic Purpura with Cyclophosphamide

To the Editor: Acquired amegakaryocytic thrombocytopenic purpura is a rare disorder occurring in adults that possesses a variable clinical course with different causes. Only a few cases have been reported in the literature. Suggested mechanisms for the disease include either an intrinsic defect in the megakaryocyte colony-form units or a circulating cytotoxic autoantibody directed against these colony-forming units. Different lines of treatment have been recommended, including corticosteroids, vincristine, and splenectomy, but they have generally been found ineffective. I describe a Yemeni patient with this disorder who, after steroid treatment failed, was successfully treated with cyclophosphamide. This may support the idea that immunological mechanisms are important in the etiology of at least some of the cases.

A 20-year-old Yemeni woman was first seen at the emergency room of Al-Salam Hospital at Sadah, Yemen Arab Republic, with a history of nasal and vaginal bleeding. She also complained of generalized weakness. She had had previous episodes of nasal and mouth bleeding and her menstrual flow was always heavy. There was no history of drug use, and family history was negative for similar illnesses.

On examination, she looked ill and marked pallor was seen over the mucous membranes. There were also multiple petechiae and ecchymoses over the entire body, but no lymphadenopathy or hepatosplenomegaly was present.

She was admitted to the hospital for further assessment and management. Laboratory analysis showed hemoglobin of 68 g/L, and white cell count of 18.5 10^9/L with 0.68 polymorphs, 0.20 lymphocytes, 0.07 monocytes, 0.03 eosinophils, and 0.02 basophils. Platelet count was 7 10^9/L. Peripheral blood smear examination showed hypochromic red blood cells, normal white cells, and a very few platelets of normal and small sizes. Bleeding, prothrombin time, and partial thromboplastin time were normal. Testing for lupus erythematosus cells and antinuclear antibody titer was negative. Hemoglobin electrophoresis showed a normal pattern and glucose 6-phosphate dehydrogenase activity was within normal limits. Chromosomal studies were normal. Bone marrow biopsy showed normal myeloid precursors, erythroid hyperplasia, and absent megakaryocytes.

Initial management consisted of platelet replacement and packed red cell transfusions, which controlled her bleeding; prednisone therapy (60 mg/day) was also started. She was discharged 10 days after admission on prednisone (40 mg/day) and ferrous sulfate (300 mg, three times a day). At the time of discharge, her platelet count was 20 10^9/L.

After this she was seen on more than one occasion in the emergency room with the same complaints. On each occasion, she was treated with packed red blood cells and platelet transfusions. Her platelet count rose adequately after each transfusion with about five units of platelets, but nasal and vaginal bleeding recurred whenever the platelet count dropped below 25 10^9/L. Four weeks after discharge from the hospital, she was readmitted from the emergency room because of severe vaginal and nasal bleeding. Her platelet count had dropped down to 8 10^9/L. Her bleeding was controlled with platelet and packed red cell transfusions but corticosteroids failed to control it. Because of this, the prednisone was tapered and cyclophosphamide treatment was started (100 mg/day). She was discharged home 10 days after the start of cyclophosphamide therapy with orders to receive platelet transfusions once weekly on an outpatient basis.

Three weeks after discharge, she was seen with a mild episode of nasal bleeding. She received platelet transfusions and the prednisone therapy was entirely discontinued. Her white cell count decreased to 3 10^9/L and thus the dosage of cyclophosphamide was decreased to 50 mg daily. She was seen on a weekly basis in the outpatient clinic, and after 8 weeks of cyclophosphamide therapy, she remained well and her platelet count remained above 150 10^9/L.

Repeated bone marrow aspiration at that time showed normal erythroid and myeloid precursors as well as normal megakaryocytes. Subsequently, and for six months, the patient was asymptomatic with platelet count above 200 10^9/L. Her most recent hemoglobin level was 132 g/L and white cell count was 6.2 10^9/L.

Acquired megakaryocytic thrombocytopenic purpura in adults is a rare disorder with a variable course[1] and different causes,[2] and only a few cases have been reported in the literature.

The differential diagnosis of patients with suspected acquired amegakaryocytic thrombocytopenic purpura should include hereditary and acquired aplastic anemia, preleukemia, systemic lupus erythematosus, and idiopathic (immune) thrombocytopenic purpura with misinterpretation of morphological findings. The patient described here had no other abnormality to suggest Fanconi's anemia.[3]

Normal myeloid and erythroid findings in both bone marrow aspirates eliminate the possibility of aplastic anemia and normal chromosomal studies rule out preleukemia. Systemic lupus erythematosus was easily eliminated because of absent clinical features and lack of lupus erythematosus cells as well as negative antinuclear antibody titer. Idiopathic (immune) thrombocytopenic purpura was unlikely because megakaryocytes were absent in the bone marrow aspirate and she responded well to platelet transfusions. Suggested mechanisms of acquired amegakaryocytic purpura include either an intrinsic defect in the megakaryocyte colony-forming cells or a circulating cytotoxic autoantibody directed against these colony-forming units.[2]

Different lines of treatment have been tried, including steroids, vincristine, and androgens, but all have been found to be ineffective. Splenectomy has also been tried, but without success. Successful treatment using cyclophosphamide was reported by El Saghir and Geltman.[4] Spontaneous recovery has also been reported.[5]

The response of my patient to cyclophosphamide treatment supports the hypothesis that acquired megakaryocytic thrombocytopenic purpura in adults may have an immunological basis in at least some of the cases, and suggests that corticosteroids and eventually cyclophosphamide or other immunosuppressive therapy as well as plasmapheresis should be tried. I believe my patient represents the first case reported from the Yemen Arab Republic.

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INTERNATIONAL SYMPOSIUM ON "DRUGS IN TROPICAL DISEASES"

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RECENT ADVANCES IN ANTIMALARIAL DRUGS, W Peters, London School of Hygiene and Tropical Medicine, London, England

The prevention and treatment of "malignant tertian" malaria due to *Plasmodium falciparum* is increasingly complicated by the rapid spread of resistance to chloroquine as well as to other widely used antimalarials such as amodiaquin, chlorguanide, pyrimethamine, and recently quinine. Since 1963 over 300,000 compounds have been evaluated as alternative drugs, mainly as part of a program conducted by the U.S. Army Research and Development Command but also under the auspices of WHO, a few pharmaceutical companies, and some governmental research bodies. Resistance also occurs in potentiating combinations of antifols containing sulfonamides such as sulfadoxine (Fansidar). Chloroquine resistance is limited to *P. falciparum* but resistance to antifols occurs in all species. Recently developed compounds already marketed are mefloquine and halofantrine. These aminoalcohols have structural affinities with quinine, and resistance to one can entail cross-resistance to all three. A new naphthoquinone, BWC566C, one of the most potent antimalarials ever developed, will shortly enter clinical trials. A new family of blood schizontocides based on artemisin, a sesquiterpene lactone described by Chinese investigators in the plant *Artemisia annua*, offers good prospects for the emergency treatment of complicated, multiple drug-resistant *P. falciparum* malaria. Several of this series are currently in clinical trial. Like multiple drug resistance in some cancers, this phenomenon is now known to be associated in *P. falciparum* with amplification of a surface protein that "exports" drugs from the parasites. Such resistance can be reversed experimentally by verapamil and by desipramine. Resistance solely to antifols is due to a mutant dihydrofolate reductase-thymidylate synthase with reduced drug affinity.

MALARIA: CLINICAL ASPECTS AND TREATMENT, O. Haddad, Security Forces Hospital, Riyadh

Malaria is one of the most prevalent and serious infectious diseases affecting inhabitants of the tropics and subtropics. More than 2.5 billion people are exposed to the risk of malaria infection with an estimated annual mortality of one million, mostly among children (1-5 years), pregnant women, and nonimmune individuals. The growing menace of drug resistance to *Plasmodium falciparum* has contributed to the evolving difficulties in the management of malaria. In spite of the spread of chloroquine-resistant malaria in more than fifty countries around the world, there are fortunately no reported cases of resistance in Saudi Arabia as yet, apart from imported cases. However, such a global spread of drug resistance makes the Kingdom, with its strategic situation between Africa and Asia, at a potential risk. The clinical course of malaria may mimic a wide range of different diseases. This ability to masquerade as other illnesses frequently contributes to the delay in establishing an early and correct diagnosis, especially in nonendemic areas. The severity of clinical presentation is dependent on the degree of parasitemia and the host immune status. Nonimmune individuals usually present with fulminant manifestation, while semiimmune typically have a milder disease. Malaria complications are commonly encountered with *P. falciparum*. Cerebral malaria, acute renal failure, and pulmonary edema are the most common causes of death. The choice of antimalarial agents depends mainly on the severity of the clinical syndrome and the pattern of the drug resistance in the community. Qinghaosu and quinine are probably the first antimicrobial agents known to medicine. Quinine is still an important drug in the treatment of severe malaria. The Chinese plant qinghao has been documented since 168BC for its antipyretic effect. The active ingredient qinghaosu (artemisin), and its derivatives are under extensive evaluation. Of a quarter of a million compounds tested for their antimalarial activity, only a few are effective against malaria parasites. Mefloquine has proved to be a valuable remedy in multi-drug resistant malaria. Halofantrine is the newest promising drug which may prove helpful in resistant cases. Further development of antimalarial drugs is mandatory to manage the increasing threat of resistant strains.

ANTIMALARIAL DRUGS, JEA Farid, World Health Organization, Alexandria, Egypt

Malaria is endemic in more than 100 countries in Africa. In its socioeconomic impact, it is the most important of the transmissible parasitic diseases. Each year some two hundred million people are infected. Of these, two million die, mostly during infancy and early childhood. Human malaria, which is transmitted by anopheline mosquitos, is caused by four species of plasmodial parasites. The most widespread are *P. falciparum* and *P. vivax*. Sporozoites, produced in the mosquito vectors from sexual forms of the parasite, migrate to the salivary glands. When injected into the blood streams of humans, they rapidly penetrate the parenchymal cells of the liver where they transform and grow into large tissue schizonts containing considerable numbers of merozoites (tissue schizogony). The tissue schizonts begin to rupture after 5 to 20 days, depending on the species, and the merozoites thus released invade circulating erythrocytes. The subsequent rapid intraerythrocytic multiplication of the merozoites (blood schizogony) culminates in the rupture of the host cells, the release of new merozoites, and the cyclical invasion of further erythrocytes which, in turn, are destroyed. The destruction of red blood cells and the release of the parasites and their waste products produce the episodic chills and fever that are characteristic of the several variants of the disease. Completion of the transmission cycle is assured because some merozoites develop into male or female gametocytes so that the host becomes a reservoir of infection for mosquitos. Certain tissue forms of *P. vivax* and *P. ovale* (hypnozoits) may persist in the liver for many months and even years. They are responsible for the relapses characteristic of these forms of malaria. Such latent forms are not found in *P. falciparum* and *P. malariae*; recrudescences of these infections result from persisting blood forms in inadequately treated or untreated patients.

QUASSINOIDS AS POTENTIAL ANTIMALARIAL DRUGS, JD Phillipson, School of Pharmacy, University of London, London, England

Species of the plant family Simarubaceae are used throughout the tropical world as antimalarials in traditional medicine. We have investigated some of these species from China, Thailand, Malaysia, India, Africa, and South and Central America for the presence of active principles. Using an in vitro test which measures incorporation of ^{3}H-hypoxanthine into chloroquine-resistant *Plasmodium falciparum* (K1) to monitor activity of plant extracts, we have isolated some 30 active compounds. All of these compounds are bitter terpenoids known collectively as quassinoids. Their in vitro IC_{50} values range from 0.0008 μg ml^{-1} (for bruceantin) to > 50 μg ml^{-1} (for cedronine). In the same test, chloroquine and quinine have IC_{50} values of 0.21 and 0.04 μg ml^{-1}, respectively. The antiplasmodial quassinoids rapidly inhibit synthesis in *P. falciparum* in vitro and there is no significant difference in their activities against chloroquine-resistant and sensitive strains. We have compared in vitro activities of quassinoids against *P. falciparum* and KB cells (human epidermoid carcinoma of the nasopharynx), and results indicate that cytotoxicity to KB cells does not necessarily parallel antimalarial activity. The in vivo activities of nine quassinoids have been assessed in mice infected with *P. berghei* (strain N, chloroquine-sensitive). All of the compounds tested orally showed some activity and one of them, holacanthone, had an ED_{90} value of 4.5 /day^{-1}/day^{-1} and killed one out of five mice tested when administered at 18 mg/kg^{-1}/day $^{-1}$. Chloroquine diphosphate and quinine dihydrochloride had respective ED_{90} values of 6.0 and 92.0 mg/kg^{-1}/day^{-1} in the same test. Selective esterification and etherification of quassinoids has resulted in a series of compounds which are currently being assessed for their in vitro activities against *P. falciparum* and KB cells.

UTILIZATION OF ANTIMALARIAL DRUGS IN SAUDI ARABIA, SM Al-Seghayer, Ministry of Health, Malaria Control, Riyadh

Malaria has long been one of the most prevalent diseases affecting the population of tropical and temperate zones. The first remedy against malaria was discovered only in the 17th century. The development of synthetic antimalarial drugs such as atebrin (mepacrine) and chloroquine forms one of the most interesting chapters in the history of malaria chemotherapy. About 1960, with the appearance of resistance of *P. falciparum* strains against the 4-aminoquinolines, there was renewed interest in developing new antimalarial drugs, hence sulfones and sulfonamides re-entered the modern history of malaria chemotherapy. New drugs such as mefloquine and halofantrine have emerged after considerable efforts to offer the best hope for success in fighting one of the world's oldest and most prevalent diseases of the tropical areas. Antimalarial drugs are wisely and beneficially utilized in Saudi Arabia to mitigate the results of malaria infection and to help control and ultimately eliminate the disease. The drugs are used in malaria control programs, in primary health care units, and in hospitals, with very limited utilization on the part of the public. The types of treatment are presumptive, radical, emergency, and prophylactic. Chloroquine, primaquine, quinine, and fansidar are usually used but others are kept in reserve.

CURRENT DEVELOPMENTS OF ANTIMALARIAL AGENTS, HY Aboul-Enein, King Faisal Specialist Hospital and Research Centre, Riyadh

Malaria is likely to remain a major worldwide health problem for decades to come. Large-scale attempts at eradication of the vector have failed, and vaccines against the various stages of the parasites are likely to take some time to develop, so that for the foreseeable future reliance on drugs for malaria prevention and treatment is likely to continue. Despite the fact that there are several new drugs under assessment, none is likely to solve all the current problems. Existing drugs are better understood now than they have been, but further work is required to improve their use. The ideal antimalarial drugs should be effective against all forms of malaria as well as nontoxic, nonteratogenic, and affordable. The major antimalarial agents currently available are (a) chinichona alkaloids: quinine; (b) 4-aminoquinolines: chloroquine, amodiaquine, sontoquine; (c) 9-aminoquinolines: primaquine, acriquine, aminoacrichin; (d) 8-aminoquinolines: primaquine, pamaquine, and others; (3) pyrimidines: pyrimethamine, trimethoprim; (f) biguanids: proguanil, chlorproguanil; (g) sulfones and sulfonamides: dapsone, sulfadoxine, sulfafurazole; and (h) quinolinemethanols: mefloquine. Recently developed antimalarial agents include sesquiterpine lactones: artemesinine and analogs; and phenanthrenmethanol: halofantrine.

NATURAL PRODUCTS AS SOURCES OF ANTIPROTOZOAL DRUGS, JD Phillipson, The School of Pharmacy, University of London, London, England

New drugs are required for the treatment of widespread protozoal infections such as malaria, amebiasis, leishmaniasis, and trypanosomiasis which affect millions of the world's population. Resistance to malaria chemotherapy has spread at an alarming rate and today it is the major infectious disease to threaten world health. Metronidazole, the major drug of choice for the treatment of amebiasis, is not well tolerated by all patients, and although resistance has not been reported, it cannot be ruled out for the future. There are no suitable drugs for the treatment of either leishmaniasis or trypanosomiasis. One obvious route to the discovery of new antiprotozoal drugs lies in an evaluation of the natural product molecules which are present in plants used in traditional medicines. In vitro tests have been used to select active plant extracts and to monitor fractionation of compounds with antimalarial, antiamebic, and antitrypanosomal activities. An in vitro test for leishmaniasis utilizing mice peritoneal macrophages infected with amastigotes of *Leishmania donovani* has been shown to be an indicator of activity for amphotericin and antimonial drugs. A number of indole, isoquinoline, phenanthrene, quinolizidine, and steroidal alkaloids have antimalarial, amebicidal, and antileishmanial activities. Terpenoid endoperoxides such as artemisin from *Artemisia annua* and yingzhaosu A from *Artabotrys unciatus* have been isolated as the active principles from these Chinese medinical herbs which are used for the treatment of malaria. Some of the bitter terpenoids including quassinoids from Simaroubaceae and limonoids from Meliaceae have antimalarial activity and a few have been investigated for activity against other protozoa. The naphthoquinones plumbagin and diospyrin are active against *Leishmania* species while lapachol is active against *Trypanosoma cruzi*. Highly methozylated flavonoids, such as artemetin and casticin, potentiate the in vitro activity of artemisini against *P. falciparum* at concentrations in which they have no antiprotozoal activity. Such findings should be followed up for potential new drug leads and those plants recommended in traditional medicine for the treatment of protozoal infections should be fully investigated for their efficacy and safety.

GIARDIASIS: CURRENT UNDERSTANDING AND TREATMENT, M Al-Tukhi, Security Forces Hospital, Riyadh

Giardia lamblia (G. doudenalis) is a flagellated protozoan parasite, in the order Diplomonadina, that has bilateral symmetry and four pairs of flagella. Three different species have been recognized: *G. agilis* from Amphibia; *G. muris* from mice, rats, and hamsters, and *G. duodenalis* from other animals. *Giardia* has two recognized stages in the life cycle. The trophozoites, which have a teardrop shape (12-13 μ by 6-10 μ), and cyst, which is 6 to 10 μ in diameter. *Giardia lamblia* causes the most recognized gastrointestinal infection among the flagellated protozoa. Many symptoms can be seen, starting with the asymptomatic stage (carrier stage) to acute diarrhea, flatulence, distention, fatigue, urticaria, arthritis, and malabsorption complications. Transmission is carried out by the fecal-oral route, through contaminated water and various vegetables. Diagnosis is not as difficult as for other protozoa. Cysts can be easily seen in simple stool examinations. In 1986, 1987, and 1988 *G. lamblia* prevalence was recorded as 40%, 14.5%, and 13.7%, respectively, of total parasites examined in the Riyadh Central Laboratories. Maternity hospital laboratories recorded the highest figures in 1987 and 1988 (68.7% and 86.7%, respectively). Security Forces Hospital laboratory recorded 25% of the total parasites seen. Several diagnostic tools are available: stool examination, examination of the intestinal fluid, small bowel biopsy, and serological test. ELISA techniques for antigen and antibody detection are developing rapidly. Treatment of giardiasis can be achieved easily by one course of treatment. However, treatment can be time consuming and frustrating due to nonresponding cases. Several drugs are available. Quinacrine (Atabrin), furazolidin (Furotone), tindazale (Fasign), orinidazole (Tiberal), and metronidazole (Flagyl). The most widely effective drug is metronidazole, and is frequently prescribed in a dosage of 250 mg tid for 7 days in adults and 5 mg/kg tid for 7 days in children. Cure rates of 65 to 90% are reported with this regimen.

ALBENDAZOLE IN HYDATID DISEASE: RESULTS IN 22 PATIENTS, I Yasawy, Armed Forces Hospital, Riyadh

A prospective study to evaluate the effect of albendazole in the treatment of *Echinococcus granulosus* was conducted at the Gastroenterology Unit, Armed Forces Hospital, Riyadh. Twenty-two patients, mainly with hydatid liver disease, were included in this study; 30% of these patients had a previous history of surgery for recurrence of previously operated hydatid cysts. The duration of treatment and follow-up period ranged between 2 months and 3 years. The only side effect was hair loss in 2 patients, which was fully reversible upon the termination of treatment. The following results were achieved: Radiological disappearances of the liver cysts were achieved in 8 patients; 4 who had ruptured liver cysts to the biliary tree were treated with a combination of a nonsurgical endoscopic method, hypertonic saline irrigation, and albendazole. In the remaining 14 patients, 5 (22.72%) had a 30 to 60% reduction in cyst size; intracystic change was noted in another 5 patients (22.72%). In 2 patients the cyst ruptured, and there was no change in the cyst size in 2 patients (9.9%). This study shows that albendazole is a promising drug for the treatment of hydatid disease.

CURE RATE STUDIES OF INTESTINAL AMEBIASIS WITH THE USE OF MITRONIDAZOLE, WITH EPIDEMIOLOGICAL STUDIES AND PREVALENCE OF THE DISEASE, MA Hafiz, Ministry of Health, Riyadh

The morphology and life cycle of *Entamoeba histolytica* and mode of infections through vegetative and cyst forms were considered along with other allied types. The prevalence of disease in Saudi Arabia in the last three years, 1406, 1407, and 1408H, was studied. Three Primary Health Care Centers in Riyadh were the sites selected for epidemiological studies and were Al-Malaz, Al-Shoubah, and Al-Marquab. The disease was studied in relation to seasonal prevalence and vector transmission. *Musca domestica* was studied in relation to the prevalence of intestinal amebiasis. Metronidazole, the drug of choice used by the Ministry of Health during 1406 to 1408 (1986-1988), was studied in relation to the cure rate. Epidemiological data on the prevalence of the disease in health provinces of Saudi Arabia described the endemicity of the disease. Data referred to the prevalence of the disease in the 3 primary care centers were defined in terms of good, moderate, and low environmental sanitation.

ENTAMOEBA HISTOLYTICA DEPRESSES CHEMILUMINESCENCE IN STIMULATED HUMAN POLYMORPHONUCLEAR LEUKOCYTES, AS Tuwajri, College of Medicine, King Khalid University Hospital, Riyadh

The effect of *Entameba histolytica* proteinase/toxin (Ehp/t) on the luminol-dependent chemiluminescence (CL) in stimulated human polymorphonuclear leukocytes (PMN) was studied. The role of superoxide (SO) and hydroxyl (OH) anions in the Ehp/t-associated enhancement/inhibition of CL was also studied using specific scavengers and a biological response modifier, muramyldipeptide (MDP). Ehp/t was isolated from axenic trophozoites of the HM-EIMSS strain of a virulent strain of *E. histolytica*. Proteinase activity was assayed on a synthetic substrate, Z-arg-arg-AFC, and cytotoxicity was tested on Hela cell monolayers. PMNs isolated from blood were incubated with Ehp/t prior to stimulation by phorbol myristateacetate (PMA, 2 μg/ml), serum-treated zymosan (2.5 mg/ml), and glucan (2 mg/ml). CL was monitored in an LKB (Wallac) luminometer. Ehp/t was found to depress up to 90% of CL induced by PMA, glucan, and zymosan. Such a depression was Ehp/concentration dependent. A 150 μg/ml concentration of Ehp/t, obtained from a 0.015 to 1.5 mg/ml concentration range tested at different incubation times and temperatures, was used in most of our experiments. Optimal incubation time and temperature were 15 minutes and 37°C, respectively. Eph/t partially inhibited the CL associated with SO and OH. MDP, in the presence of Ehp/t, enhanced CL response in human PMN to about 67% with reference to normal CL without inhibitor. PMNs were confirmed to play a vital role in amebic tissue invasion mechanisms.

THE GENUS LEISHMANIA IN SAUDI ARABIA, W Peters, London School of Hygiene and Tropical Medicine, London, England

Cutaneous leishmaniasis ("Al-Okht," CL) has long been known to occur in Saudi Arabia and at least 20,000 cases a year are recognized. The common occurrence of visceral leishmaniasis (kala-azar, VL) in the southwest has only been acknowledged recently and the problem is increasing. New techniques for the biochemical identification of *Leishmania* have made it possible to correlate clinical and epidemiological observations. A team from King Faisal University supported by KACST and staff of the Ministry of Health working with UK investigators have now shown that at least five species of Leishmania and one hybrid form exist in the country. CL due to *L. major* occurs as a zoonosis in semi-desert lowland areas, especially around newly constructed dwellings that impinge on the cycle of transmission by the sand fly, *Phlebotomus papatasi*, between rodents, mainly *Psammomys obesus*. Feral dogs may also be infected. In the Asir highlands above about 1800 m, CL due to infection with *L. tropica* is transmitted by *P. sergenti* and is probably anthroponotic. In the Eastern Province (and probably in areas of the Middle East with a similar etiology), *L. arabica* is not pathogenic for man and a naturally occurring hybrid between this and *L. major* has been discovered in rodents and feral dogs. Infantile VL, occurring among inhabitants of the western slopes of the Asir range below about 1600 m and in the Tihama, is due to an unnamed parasite of the *L. donovani* complex but, in the same areas, feral dogs are commonly infected with typical *L. infantum* which has also been identified in an infant in neighboring Yemen. With more accurate knowledge of the parasites and their epidemiology, specific control measures can be designed in a logical manner.

ETIOLOGICAL AGENTS, TREATMENT AND PREVENTION OF LEISHMANIASIS IN SAUDI ARABIA, MA Al-Zahrani, Ministry of Health, Riyadh

The term "leishmaniasis" is a misnomer since it embraces a variety of clinical syndromes that are, in turn, the outcome of infection with a wide variety of parasite protozoa within the genus *Leishmania*. Only recently has it been accepted that certain species of Leishmania respond poorly to standard antileishmanial drugs and also that there can be considerable differences in the response of isolates of particular parasites from different geographical areas. In Saudi Arabia, the cutaneous form of leishmaniasis is due to infection with one of two parasites, *L. major* and *L. tropica*. Infantile kala-azar is due to infection with *L. donvani* sensulato zymodem LON-42. The distribution of these species in Saudi Arabia was discussed. The problem has been how to distinguish the parasites, not only at the species level but also at the level of such variations as response to drugs, antigens, and clinical outcome of infection. A variety of biochemicals are now becoming available with which to differentiate the *Leishmania*, most of which are impossible to identify on purely morphological grounds. The mainstay of therapy for all types of leishmaniasis remains the pentavalent antimonials, sodium stibogluconate (Pentostam), and meglumine antimonate (Glucantime). Many claims have been made for the efficacy of a wide variety of other drugs and alternative forms of other therapy were discussed. In the absence of good effective vaccines and chemotherapy for the prevention of leishmaniasis, control of these infections depends on measures aimed at the vectors and/or reservoir hosts, where these are known.

CUTANEOUS ADVERSE REACTIONS OF DRUGS USED IN TROPICAL DISEASES, HA Jamal-Eldin, Maternity & Children's Hospital, Jeddah

Systemically administered drugs can produce a number of morphologically distinct cutaneous symptoms. After discontinuation of the medication, the symptoms usually regress. The literature about undesirable drug reaction has increased rapidly during recent years. These reactions are seen most commonly in the skin, and among these, macular eruptions and urticaria have the highest incidence. The cutaneous manifestations of drug reaction vary widely in severity. They are generally mild and transient, but can lead to severe systemic illness and may, on occasion, be fatal. In the differential diagnosis of macular and maculopapular drug eruption, difficult problems may be present, e.g., viral exanthematous diseases and some additives that may be contained in medications. So, this study was designed in a trial to increase awareness of physicians about the cutaneous side effects of some drugs that can be used in the management of some tropical diseases, e.g., antimalarial, antiamebic, and antibilharzial drugs.

EPIDEMIOLOGICAL PATTERNS OF CUTANEOUS LEISHMANIASIS, M Al-Shabrawy, College of Medicine, King Saud University, Riyadh

Five hundred (500) patients with variable leishmanial skin lesions attending the dermatology clinic at the King's Hospital, Al-Kharj, over a period of 16 months from Muharram, 1405H, to Rabi Ul-Thani, 1406H, were analyzed. The study revealed that infection is far greater among non-Saudis (93%). The Saudi patients comprise only 7% of the cases. Most of the Saudi patients (70%) were children less than 10 years of age. Ninety-two percent of the patients were agricultural laborers living on farms. Lesions were seen mostly on exposed parts of the body, such as the face and upper and lower limbs. The number of lesions in Saudi patients were less than those in non-Saudi patients. Eighty-five percent of the Saudi patients did not have more than three lesions. The infection was found to be seasonal, with most cases found in winter. Sodium stibogluconate (Pentostam) injections have been used for treatment of the patients, and variable courses have been attempted. Available drugs (rifampicin, isoniazid, trimethoprim, sulfamethoxazole, ketocozole, intralesional steroids, and levamisole) have been tried with variable results. A controlled therapeutic trial is required to answer many queries regarding efficacy.

ORIENTAL SORE: A THERAPEUTIC CHALLENGE, Y Al-Gindan, King Fahad Hospital of the King Faisal University, Al-Khobar

Oriental sore (OS) is a self-healing process. This makes assessment of any type of management complicated. The duration of the disease is long. The clinical presentation is variable and may result in an ugly scar. Major objectives in the management of OS are to influence the course of the disease by shortening its duration and improving the cosmetic result of its scar. Various drugs have been tested in the management of OS. This includes both local and systemic applications. Unfortunately, none of the drugs used seems to be ideal. Our experience in a field study with three threatment modalities in the management of OS was presented.

EPIDEMIOLOGY AND CONTROL OF SCHISTOSOMIASIS IN SAUDI ARABIA, AK Al-Madani, College of Medicine, King Saud University, Abha

Schistosomiasis control operations carried out during 1983 to 1988 were described briefly, together with available information on the impact of schistosomiasis. The prevalence of schistosomiasis has declined from 9.5% in 1983 to 1.8% in 1988 ($P < 0.05$). The infection occurs more frequently in Saudis than in non-Saudi expatriates and in males more than females. Schistosomiasis mansoni is more prevalent than *Schistosomiasis haematobium*. The fall in prevalence of *Schistosoma mansoni* was 51.5% but that of *S. hematobium* fell by 78.5%. *Bilinus truncetus, B. becoarii*, and *B. reticulatus* wrighti are the intermediate host of *S. mansoni* and are found wherever the disease is endemic. The influx of expatriate workers arriving from endemic countries with schistosomiasis, the inaccessible water sources, the constant movement of large numbers of bedouins in some regions, and the manpower shortages in some regions are considered to be the main obstacles to schistosomiasis control programs in Saudi Arabia.

IMMUNOPATHOLOGY OF SCHISTOSOMIASIS, AK Tawfik, College of Pharmacy, King Saud University, Riyadh

Schistosomiasis is one of the most widespread parasitic diseases in the world. More than 200 million people are infected with schistosomes, and approximately 500 million persons are exposed to the possibility of infection. The clinical manifestations of schistosomiasis can be categorized to the stages of its life cycle. Swimmer itch is a syndrome which develops upon repeated exposure of humans to non-human schistosomes. It is a dermatitis mediated through type III of hypersensitivity. The acute stage is characterized by granuloma formation surrounding the schistosome eggs trapped in the liver or in the bladder, depending on the species. These granulomas are the result of strong cell-mediated immune response mounted to the released egg antigens. The chronic stage of the infection emerges as the number of accumulating granulomas progresses. This may lead to hepatosplenomegalic diseases. This report discusses the immunological responses involved in the pathogenesis of schistosomiasis and how these responses contribute to protection.

PROGRESS IN THE THERAPY OF SCHISTOSOMIASIS, F Sharabi, Security Forces Hospital, Riyadh

Schistosomiasis (bilharziasis) is a major worldwide health problem that is particularly problematic in less developed countries where the disease causes a substantial economic burden. Over 200 million people are believed to harbor the parasite. It is a visceral parasitic disease caused by blood flukes which undergo a special life cycle. Infection results in a debilitating disease with various clinical signs and complications. An overview of the chemotherapy is presented to describe the properties of the antischistosomal drugs, mechanisms of action, uses, and the response of the parasites to these agents. The history of chemotherapy for schistosomiasis has been characterized by a prolonged monopoly of the antimonials, followed by an exciting period of events that have significantly modified the approach for the control of the disease. The chemotherapy commenced more than 70 years ago, when tartar emetic was tried in Khartoum in 1918. Since that time, because of the toxic effect of antimonials and the search for orally active drugs, 250,000 substances were screened for antischistosomal activity. A series of new compounds came into practice: lucanthone (1948), metrifonate (1962), Niridazole (1964), hycanthone (1965), oxamniquine (1969), and finally praziquantel (1975). Praziquantel has proved to be a major therapeutic advance, being orally effective, safe, well tolerated, and of broad-spectrum activity. Undoubtedly it has become a drug of first choice, and thus appears to have ideal properties for the treatment of schistosomiasis.

CYTOTOXIC NUCLEOSIDES: USE AGAINST SCHISTOSOMIASIS AND OTHER PARASITES, HP Baer, King Faisal Specialist Hospital and Research Centre, Riyadh

Cytotoxic nucleosides such as tubercidin are powerful antiparasitic agents, but they are also very toxic to mammalian cells. Recent understanding of the mechanisms of nucleoside transport across membranes, which largely occurs by facilitated, carrier-mediated diffusion, has led to the discovery that parasites possess transporters distinct from those of mammalian cells. In particular, the latter are selectively inhibitable by a number of drugs which are ineffective in parasites. Thus, the combined administration of tubercidin with a mammalian nucleoside transport inhibitor protects the mammalian host cells against the cytotoxic tubercidin but leaves the parasites fully exposed. Excellent therapeutic results have been obtained by us and others in cases of experimental schistosomiasis in mice (*S. mansoni, japonicum, haematobium*) with elimination of worms and egg production. This combination treatment principle may prove to also be effective against other parasitic diseases. A major requirement for clinical acceptance of this regimen is reliable, effective host protection. Our recent work has been directed toward the search for host-protecting nucleoside transport inhibitors with favorable pharmacodynamic properties. Particularly promising seem to be a number of mioflazine derivatives (Janssen Pharmaceutical) which have proven to be effective in vivo and in vitro, including as host protectors against tubercidin toxicity in mice. Since these drugs are under clinical development for other purposes, the clinical testing of an antiparasitic combination treatment regimen would be much facilitated.

COMPARATIVE STUDY: COST EFFECTIVENESS OF METRIFONATE AND PRAZIQUANTEL CHEMOTHERAPY IN SCHISTOSOMA HEMATOBIUM MASS, M. Foda, Primary Health Care, Tabuk Health Region, Tabuk

In view of universal limited resources in the health sector, specialized schistosomiasis mass chemotherapy control programs can only be justified if their evaluation demonstrates their cost effectiveness. In order to analyze the cost effectiveness of our mass chemotherapy program, a model was used to compare the treatment of urinary schistosomiasis with metrifonate (three-dose regimen at fortnightly intervals) and praziquantel (one-dose regimen). The model was applied to two situations: village I where the average distance between the project base and the area of intervention was 100 km, and village II where the average distance was 300 km. The aim of the project was to reduce the prevalence of infection from 50% to about 3%. The cost of the project was not only determined by drug expenditure but also by operation cost as well as drug effectiveness and side effects. Using metrifonate, the cost per person rendered negative was $7.79 and 20.56 in village I and II, respectively, and the prevalence was 3.2% after the fourth mass treatment. The cost of praziquantel was $4.55 and 6.57 for village I and II, respectively, and the prevalence was 0.8% after the second mass treatment. There were no observed serious side effects for either metrifonate or praziquantel. The cost difference was mainly due to high operational cost, incurred by the three-dose regimens because metrifonate is much cheaper than praziquantel. Once low prevalence levels are reached, operational cost would further outweigh drug expenses.

FOURTH ANNUAL HEALTH CARE MANPOWER DEVELOPMENT SYMPOSIUM ON NURSING: THE FUTURE CAREER CHOICE

Sponsored by the King Faisal Specialist Hospital and
Research Centre, Riyadh,
3 - 4 October 1989

PREPARATION, EMPLOYMENT, AND TRAINING OF NURSES IN CIVIL SERVICE, A Al-Abdulqader, Civil Service Bureau, Riyadh

The following topics were discussed: (1) the situation of nurses before entering civil service through preparation at all different levels; (2) employment in the civil service sector; and (3) developing and improving nurses's performance and productivity through training. The paper will study the present situation, problems confronted, and future outlooks for each topic. The great concern paid to such elements and factors became as a result of deep relationship and mutual effects, as preparation affects recruiting personnel in the suitable field of work. Training also contributes greatly in promoting efficiency and improving performance.

A RESEARCH MODEL FOR THE INVESTIGATION OF THE DETERMINANTS OF THE SAUDI NURSE SHORTAGE, AM Al Haydar, Institute of Public Administration, Riyadh

This paper proposes a research model for investigating factors affecting participation of Saudi women in the nursing field. Saudi women represent only 4% of the Ministry of Health nursing force in hospital-based and primary health care. A clear understanding of the pertinent factors and their interaction will allow targeting the areas concerned to ameliorate the current shortage and focus efforts on relevant areas. It has been suggested that social factors, economic factors and incentives, education factors, and factors pertaining to the nature of the nursing profession may be important determinants in the lack of interest on the part of Saudi women to pursue a long-term commitment in the nursing field. An integrated perspective is adopted to study these barriers. The approach views the Saudi nurse shortage as a joint function of the domains of the social, economic, and educational factors, and the nature of the nursing profession. The relative importance of each of these four factors must be determined in order to understand the nature of the problem concerning enrollment of Saudi women in the nursing profession. The analysis plan for this model relies on Linear Structural Relations (LISREL), a statistical technique for analyzing data according to specified causal linkages. The LISREL model is based on a general model having two components. First, the measurement model that specifies the relations between observed variables and unobservable theoretical constructs. The four constructs in this proposal, i.e., social, economic, educational, and nursing nature, are each indicated by measurable variables. For example, the construct of social factors may be indicated by such observed variables as work, and society's perceived view of nursing. The second component is the Linear Structural Equation model which specifies the causal relationship between the four constructs and the dependent variable, i.e., Saudi nurses. This proposal model is expected to provide a clear picture of the major factors contributing to the nursing shortage and will ultimately affect the enrollment of Saudi women in the field.

NATIONAL MANPOWER REQUIRED FOR THE HEALTH CARE SECTOR WITH SPECIAL EMPHASIS ON NURSING, H Mansour, Manpower Council Secretariate General

Exploring the available potentials and manpower requirements needed for the health sector is a basic factor in drawing future plans for this sector, and in determining its utmost priority as compared to the other sectors of the national economy. This is particularly true in a country such as the Kingdom of Saudi Arabia, which is characterized by the scarcity of its national manpower and the availability of an international market that can provide it with the needed manpower with diversified expertise. When dealing with the problem of national manpower planning for the health sector in the Kingdom, we face the fact that there are various areas characterized by extreme shortages and imbalance in certain categories of national manpower, such as nursing. This research paper highlights the current status of manpower in the health sector, with special emphasis on nursing. It focuses on the following points: current and expected requirements; national manpower currently available and numbers that could become available to satisfy such requirements; training programs required for nationals to qualify them to work in the health sector, including the various nursing fields; and methods to be followed in order to close the gap between demand and supply as regards the technical national manpower for the health care sector generally, and nursing particularly.

INTERNATIONAL DEVELOPMENT WITHIN NURSING, DS Quinn, Former President, Royal College of Nursing of U.K., EEC Advisory Committee on Training in Nursing

Nursing has a major international forum in the Quadrennial Nursing Congress held this year in Seoul, Korea, and organized by the International Council of Nurses. Major issues and developments are discussed here, and work is carried out by the ICN between meetings so that nurses have the opportunity to know what is happening in nursing across the world. This paper discusses briefly some major areas of development and concern which are current issues. In the field of *Clinical Practice*, quality assurance in standards of nursing care is highlighted, along with the increasing trend to specializations among nurses, both moving alongside medical specialties and in newer nursing roles such as the nurse practitioner and clinical specialist. The importance of the *Regulation of Nursing* is mentioned, and the recent project and workshops of the International Council of Nurses on the subject. In *Nurse Education*, I attempt to trace the change from an apprenticeship-type training to an academically acceptable education with universities and colleges of high education. The trend to the latter is almost universal although there are variations in methods. *Primary Health Care* is viewed in relation to the World Health Organization goal of Health For All by the year 2000, and the way this has resulted in WHO acknowledging the nurse's role and the subsequent WHO Report on "The Role of Nursing and Midwifery Personnel in the Strategy of Health For All," which demonstrated the critical situation in most countries and led to a resolution being adopted by the World Health Assembly in 1989. The major part of this paper is concerned with *Nursing Manpower*, pointing out how the other developments mentioned have an effect on nursing manpower. The diminishing pool of qualified nurses and of students is described, together with some of the problems of salaries and working conditions. Changes in nursing education which remove students from a service-giving role gives rise to a shortage of nurses in the short term. The United Kingdom is just beginning this transition, and there is a brief description of how attempts are being made to quantify the difficulties and find solutions. Finally, there is a brief look at how the worldwide nursing shortage can affect the Gulf States, which rely so much on expatriate nurses, and some tentative suggestions as to solutions, while recognizing that this can only be solved by the country itself. Documents of the World Health Organization and the International Council of Nurses were drawn on in the preparation of this paper.

ANALYTICAL STUDY ON THE SHORTAGE IN SAUDI FEMALE NURSING STAFF, MH Al-Osemi, College of Applied Medical Sciences, King Saud University, Riyadh

Tracing the development and progress in the field of health care in Saudi Arabia reveals amazing achievements. The Ministry of Health was established in 1951, with 3 hospitals and 200 beds. By 1986, there were 142 hospitals affiliated with the Ministry of Health alone (capacity, 24,242 beds), in addition to 1340 health centers serving various regions of the Kingdom. According to the 1986-1990 plan, the Ministry of Health will provide 9,000 more beds, 880 health centers, and 100 maternity and child care centers. In 1979, Saudi Arabia had a population of 8.6 million, with an annual increase of 3.6%. By 1999, the number could increase to 20 million. The average age has increased to 62. Therefore, the need for health care for expectant mothers, children, and the elderly is increasing, and more health and special centers must be established. Health care in the Kingdom depends on a system of comprehensive service, requiring the Ministry of Health to provide buildings, a work force, and equipment. The development of technology and medical sciences further increases the need for health services. Training and recruitment of the work force is very important, and the nursing staff is one of its most important categories. In 1986, there were 1,980 Saudi nurses working with the Ministry of Health, and 22,548 non-Saudi. Per the Kingdom's Fifth Development Plan, the Ministry's need for nursing staff will reach 10,000. The Kingdom currently depends on non-Saudi nurses; many other countries also suffer from the reluctance of female and male youths to join nursing as a career. The Ministry of Health and the Ministry of Higher Education became aware of this situation years ago, and in 1379H, health institutes were established; there are currently 31 institutes for boys and girls in various regions of the Kingdom. Further, the Ministry of Higher Education has established two nursing colleges since 1396H, to graduate nurses with university degrees. The number of graduates from both levels, however, does not satisfy the needs of the Kingdom. This shortage is due to reasons to be discussed in this study, seeking appropriate proposals and solutions. The main points to be analyzed are: (1) the level of nursing education in the Kingdom; (2) nursing teaching and training; (3) means of attracting females to choose nursing as a career; (4) the curriculum and teaching staff; (5) employment planning; and (6) team work in nursing.

FIELD RESEARCH ON THE WORKING SAUDI FEMALE NURSE, S El-Zahrani et al, Director General for Health Institutes, Ministry of Health

The objectives of this study were to: 1. Study reasons why some Saudi nurses refuse to work in a hospital and prefer to work in the health center, and to plan for the future to solve this problem. 2. Find ways to encourage Saudi nurses to work in hospitals, especially in the gynecology/obstetrics department, and to work all hospital shifts including night duty. 3. Study the views of the director, who is responsible for the Saudi female nurse, for the improvement of the educational, practical, and job status. 4. Find ways to encourage health institute graduates to continue working in the nursing profession. The study included a questionnaire to be filled out by: (1) Saudi female nurse, to get her opinion regarding her profession, (2) the director, who is responsible for the Saudi female nurse, (3) the patient in the outpatient department, who has previously dealt with both Saudi and non-Saudi nurses. The study is not completed, and results will be presented at the Annual Health Care Manpower Symposium. Two researchers were chosen from all areas of the Kingdom to collect data from all Saudi female nurses working in the Ministry of Health. The number of Health Institute graduates since opening the Institute (1383-1384H until 1408H) was 1,900 nurses from the following areas: Riyadh, El Gassim, El Taif, El Madina, Gizan, Makkah, El Hassa, Assir East, Jeddah, and north. The data of the study will be analyzed by computer into sample frequency distribution with number and percentages.

CENTRE FOR EXCELLENCE: BUILDING NURSING IMAGE IN SAUDI ARABIA, BJ Brown, Associate Executive Director, Nursing Services, King Faisal Specialist Hospital and Research Centre, Riyadh

The worldwide nursing shortage presents various concerns for the future provision of nursing care for the people of Saudi Arabia. Many factors contribute to the nursing shortage. While wage and salary issues are always important for each employee, the appropriate utilization of nursing resources is essential to developing a center for excellence and improving the image of nursing. The nurse's time should be utilized in as much direct patient care as possible by providing adequate staffing levels for clinical and nonclinical support services. The practice environment should foster greater representation to participation of the nursing professional staff in decision-making activities. Innovative nurse staffing patterns that recognize and appropriately utilize the different levels of education, competence, and experience among nurses are essential to creating a center for excellence. The use of automated information systems and other new labor saving technologies as a means of better supporting nurses to ensure cost effectiveness in practice settings, appropriate clinical decision making, authority of nurses in relationship to other health care professionals through collaborative practice committees, and better health care team communication systems ensures that the appropriate provider delivers the necessary care. Developing continuing education programs, which allow for advancement in the practice settings, ensures upward mobility for nurses. Creation of a comprehensive professional practice environment which enables nurses to be used to the fullest for direct patient care, a positive and accurate image of the profession and the work of nurses will be promoted in Saudi Arabia. In the primary nursing model, nurses identify all functions performed and those which can be delegated to lesser prepared individuals. This provides a new care model that clearly identifies patient care functions and the responsibility of the nurse for assuring the quality of patient care. When nurses are recognized for their achievement, participate actively in clinical decision making, are utilized according to their level of competence, and are given the opportunity for professional growth through strong educational programs, the quality of patient care increases significantly and a center for excellence in nursing practice is possible. The patient is able to see the difference in the quality of nursing care and recognizes those who perform with clinical excellence.

THE IMAGE OF THE NURSING PROFESSION: STRATEGIES FOR CHANGE, S Mokabel, Head of Nursing, University of Alexandria, Egypt

All professions including nursing rest on a cultural base. Socialization, the process of learning basic values that prepare individuals to fit into their cultural milieu, contributes to the cognitive system a collection of interrelated items of knowledge and beliefs about the profession of nursing. Consistency between the knowledge, ideas, and beliefs about nurses and the actual role, work, and nature of nursing yield an ideal or consonant image. The absence of such consistency and the ensuing internal contradictions provide a cognitively dissonant image of nursing. When this theoretical model was empirically tested on a group of nurse educators, the resultant incongruity between their attitudes toward professionalism in nursing and their role orientations yielded strong evidence that improving the nursing image entails changes in the attitudes and beliefs of the nurses themselves. The study was conducted at the University of Alexandria. All nursing faculty (80) employed at the nursing institute were included in the study. An attitudinal rating scale was employed to assess the sample attitudes toward the attributes of the nursing profession. The results obtained provide a fuller understanding of both the complexity of the image issue and of the strategies that can be useful in effective change. Emphasis is placed on the important role the nurse educators have in shaping attitudes and beliefs of the public at large, and the students entering the nursing profession.

SOCIAL FACTORS AND THEIR IMPACT LOCALLY ON NURSING AS A PROFESSION, K Nasser, Chairperson, Nursing Department, Faculty of Medicine and Allied Sciences, King Abdulaziz University

The role played by religion in enhancing this noble profession and drawing support for it: Historical development of the discipline of nursing, before Islam and after Islam. Female Arab nursing at the early period of Islam. Koaiba Bint Saad Al Aslamia (Rofaida), Nosaiba Bint Kaab Mademia, Om Senan Al Eslamiya, Om Matawee Al Alamiya, Rofaida Prize, Foundation of the discipline of nursing on persons; society; and health. Influence of the family and schools in the early stages on the selection of nursing as a profession at present and in the future. Family functions: the family has been able to influence and change society's values, attitudes, and effective function. Socializing and social placement function. Health care function, reproductive function, and economic function. Report of an opinion survey of the Saudi family's attitude toward the nursing profession at King Abdulaziz University School's role and influence. The role played by news media in enhancing the image of this profession in order to increase the number of students willing to join this profession. The media communicates the message and helps to form public opinion: newspapers; radiobroadcasting; television; video; and magazines. Special programs to improve the image of the nursing profession should be part of the comprehensive plan. Role of concerned institutions in promoting the nursing profession. Social systems that might share in the promotion of the nursing profession. Education, communication system, welfare system, and recreation system.

THE CURRENT SITUATION OF THE NURSING MARKET IN JORDAN, WA Suliman, Chairperson, Nursing Department, University of Jordan

This investigative study focused on the nurse shortage in Jordan, and on the strategies that have been employed to overcome the problem of this nursing shortage. Among the three strategies that have been carried out, two strategies, recruitment of non-Jordanian nurses and the establishment of short nursing education programs that prepare practical nurses, were not successful in providing quality nursing care. The third strategy, the expansion in the registered nursing education program (BSN, Diploma); was successful in attracting more applicants to nursing education, and therefore decreasing the shortage of registered nurses in the country. However, the problem in the last year remains how to keep registered nurses in the profession. The underlying reason was the devaluation of the Jordanian Dinar which has increased the mobility of registered nurses to sister Arab countries. It was recognized that unless self-sufficiency among all Arab countries is reached, the problem of the nursing shortage in Jordan will not be solved.

SAUDIZATION OF NURSING: DIFFICULTIES AND SOLUTIONS, R Aba-Alkheil, Director of Quality Assurance, Security Forces Hospital, Riyadh

There is no doubt that there is a dire need for all specialized personnel in the health care field, especially nursing personncl, to provide the sophisticated health care that the Kingdom of Saudi Arabia is experiencing and aiming for, in all areas. The care and attention that the Kingdom of Saudi Arabia has paid to the well being and health conditions of its citizens started 30 years ago, when in 1961, the World Health Organization sent Dr. Soad Hussein to study the possibility of opening nursing schools, as requested by Dr. Hussein Nassif, the Minister of Health at that time. Based on the field study and interviews with Saudi females, two schools for nursing were established, one in Riyadh and another in Jeddah. During the last three decades, nursing education has developed tremendously. There are two colleges of nursing in Jeddah and Riyadh, and 29 nursing institutes for males and females. The social view toward nursing comes short of Islamic outlook. Also, mass media has helped in reinforcing the negative image toward this noble profession by not showing the appropriateness of a working atmosphere in a hospital which does not conflict with the culture and Islamic teachings. Also, lack of first aid programs in early stages of education, combined with absence of awareness, are contributing factors to the people's conception of the nursing profession. Unsuitability of working hours, and lack of support services, such as transportation and day care centers, are secondary factors contributing to the shaping of this social attitude. Therefore, in order to improve the present nursing situation, the following are some recommendations that I envision will create the appropriate atmosphere for Saudi nurses and will increase the number of Saudis joining this noble profession: (1) Through mass media: spread public awareness and clarify the right image and outlook of the nursing profession and its importance and (2) Through religious leaders: point out the importance of the nursing profession and encourage people to join it. None of these factors can function independently. Therefore, it is important that all efforts of institutions, government agencies, and the people be combined and coordinated in order that they may function and fulfill their roles.

NURSING SHORTAGE IMPACT ON SAUDI ARABIA: STRATEGIES FOR THE FUTURE, A Al-Ammari, Executive Director, Hospital Operations, King Faisal Specialist Hospital and Research Centre, Riyadh

Nursing is a resource that is integral to the health of the people of the Kingdom of Saudi Arabia. The reported international shortage of registered nurses is real, widespread, and of significant magnitude. The worldwide nursing shortage, which impacts all health care delivery settings and all nursing practice areas, must be considered in the future planning for health manpower, to faster self-sufficiency within the Kingdom of Saudi Arabia. There is an increase in demand for nurses, especially in the critical care and very highly specialized areas of nursing practice. Declines in admissions, enrollments, and graduations from nursing programs in other parts of the world suggest that the future of the nursing supply in Saudi Arabia will be problematic. The shortage of nurses will affect the quality of patient care and the work environment for nurses, and the access to health services by the people. It is essential that Saudi Arabia address the development of a nurse supply from the standpoint of future students and future careers. A survey conducted by King Faisal Specialist Hospital of 302 male students and 687 female students in university and secondary schools in the Riyadh area provides insight into the future career goal aspirations of current Saudi students. A second study, with general response from secondary school students in the Riyadh area, with 261 males and 355 females participating, revealed student opinions regarding employment opportunities and attitudes toward nursing as a profession. Increased public awareness regarding nursing as a career can contribute positively to attract students into Saudi nursing education programs. Additional education and training programs of expatriate nurses to provide for incresed specialization in critical areas of need will also assist with meeting the demand for qualified nurses to improve the quality of patient care. Proper utilization of nurses on the job, improved working relationships to involve nurses in decision-making, and development of a professional nursing practice environment are effective strategies to attract and retain nurses.

HOSPITAL-ATTACHED NURSING SCHOOLS: AN ALTERNATIVE FOR SAUDI ARABIA, MH Ayoub, Director of Health Region, Al Hassa

The existing nursing education system has become less effective in supplying hospitals and other health institutions in Saudi Arabia with well-trained nurses. The graduates, after three years of training, feel they are not equipped with sufficient knowledge and the skills required for the job, despite being trained in separate schools. The graduates feel they are not trained to do nursing jobs, but only to pass the examination. The training of nurses should provide more clinical exposure in general hospitals in order to attain the following objectives: (1) The trainee will be familiar with the hospital environment. (2) The training will be based on the nature of the nursing job and will be task-oriented. (3) The training will be done with people who really practice nursing care. I have surveyed approximately seventy nurses working in hospitals and public health centers to support my theories. The results will be summarized and illustrated in the conference.

ATTITUDE OF SAUDI FEMALE PREPARATORY AND HIGH SCHOOL STUDENTS TOWARD NURSING, SA Assuhaimi, Assistant Professor, Family and Community Medicine, King Faisal University

This study aimed at exploring the attitudes of Saudi female preparatory and high school students towards nursing. The specific objectives were to explore the thinking of those students considering a nursing career and of those who definately intended to become nurses. Another objective was to explore the reasons for accepting or rejecting the idea of becoming a nurse. It was also planned to examine factors influencing these attitudes. A one-page, self-administered questionnaire was the tool for this research. Four schools (two high schools and two preparatory schools) in Al Khobar town in the Eastern Province of Saudi Arabia were chosen. One class from each level in each school was chosen randomly, and all Saudi students in these classes were included. In general, one-third of the female students had positive attitudes toward nursing as a profession. "Working with males" was the main objection. This was followed by, "not suitable for girls," and "hard job," and "family objections." Viewing nursing as a "humane" profession was the main incentive for becoming a nurse. The other main reasons were, "need of the country for nurses," and as a source of personal income.

ORIENTING NURSING PROFESSIONALS TOWARD PRIMARY HEALTH CARE, Y Al Mazrou, Director General of Health Centres, Ministry of Health

The majority (98%) of the nursing professionals in the Ministry of Health are derived from the expatriate population and these nurses possess a varied past primary health care exposure, either obtained during formal training or by experience. Primary health care orientation, through inservice training, was the chosen alternative for fulfilling the cherished dream of primary health care in Saudi Arabia. The processes in such training had to include reorientation in culturally acceptable ethical practices and innovative communication skills, in addition to the principles and methods of primary health care practices. Details were given on the basic primary health care orientation package, category training, in-depth selective training, its content and extent, and how this informal inservice training was instrumental in establishing a strong primary health care base in Saudi Arabia as observed by the recent (1989) WHO/MOH joint review mission. It is hoped that primary health care will be introduced in the curriculum of local nursing education. It is important that the training process be continued, not only to maintain the achieved quality of primary health care nursing but also to cater to the ever-increasing need for new entrants.

ANNUAL PATHOLOGY SYMPOSIUM: PATHOGENESIS OF INFECTIONS IN THE COMPROMISED HOST

Organized by the Department of Pathology,
King Faisal Specialist Hospital and Research Centre, Riyadh
31 October - 1 November 1989

MAKING OF A COMPROMISED HOST, PB Herdson, Pathology Department, King Faisal Specialist Hospital and Research Centre, Riyadh

Immunity and immunological disorders are to comtemporary medicine what bacteriology and bacterial diseases were to medicine at the turn of the century. For the past few years, we have seen newly described diseases, new insights into the causation of old diseases based on increasing knowledge of immunology, and new modes of treatment based on immunotherapy. It has become apparent that on the one hand man is dependent for his survival on his immune system, while on the other he is vulnerable to a wide range of disorders resulting from its dysfunction. At one end of the spectrum, we have immune deficiency states (primary or secondary) which render the patient easy prey to infectious diseases. And at the other extreme, a hyperactive immune system can react against self to cause a range of autoimmune diseases. The term "compromised host" relates to a person who is less than normally able to resist infection, owing to primary or induced disorders of the immunological system, severe anemia, severe burns, and other major damage to protective barriers, or concurrent disease including metastatic malignancy or severe malnutrition. In this symposium, emphasis was placed on the immunocompromised host, dealing more with those patients suffering from secondary immunodeficiencies than with those experiments of nature known as primary immunodeficiency states.

THE ROLE OF NORMAL FLORA IN HEALTH DISEASE AND NOSOCOMIAL INFECTION, JD Williams, Department of Medical Microbiology, The London Hospital Medical College, London, England

The normal flora of the body is distributed superficially—on the skin and mucous membranes, and internally—in the gastrointestinal tract. These organisms provide many beneficial functions to man, not the least being the prevention of colonization of surfaces and the intestinal tract by more pathogenic species. Ways in which the normal flora can initiate disease include the following: (1) translocation from carrier sites to internal organs such as viridans streptococci to heart valves in endocarditis; (2) implantation of normal flora into normally sterile sites during surgical procedures, particularly if a foreign body is present; and (3) invasion of an immunocompromised host during, for example, neutropenic episodes while receiving anticancer chemotherapy. In addition, patients in hospital often acquire new bacterial species to add to their existing normal flora. The new species are invariably more antibiotic-resistant than the species they replace. Therefore infections with "nosocomial" normal flora are more difficult to treat.

DYSFUNCTION OF NEUTROPHILS, LYMPHOCYTES AND MONOCYTES, GT Roberts, Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

The participation of leukocytes in host defense is a complex process that involves not only their intrinsic function but also their interaction with other leukocyte types, mediated either by direct contacts or through the action of various humoral agents. Disturbances of leukocyte function are therefore complex, although not all defects will lead to significant clinical conditions. Many of these disorders are inherited or congenital, but others are acquired through injury by either physical or biological agents. In general, disturbances of function of each individual cell type result in certain patterns of susceptibility to infection that can provide a clue as to the underlying problem in each individual case. For example, the pattern of infection in patients with so-called chronic granulomatous disease points to a defect in oxidative metabolism in granulocytes and monocytes. Likewise, the pattern of some of the lymphocyte defects such as X-linked agammaglobulinemia show clinical features that suggest the nature of the defect. The molecular biology and autogeny of some of these disorders was reviewed.

INFECTIONS IN BONE MARROW TRANSPLANT RECIPIENTS, KV Sheth, AM Tulbah, R Binladen, Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

From March 1984 to July 1989, a total of 157 allogenic bone marrow transplants were performed at KFSH&RC. The clinical diagnosis of patients prior to transplantation included acute myelogenous leukemia in first remission, 39; chronic myelogenous leukemia in chronic phase, 34; aplastic and Fanconi's anemia, 32; acute lymphocytic leukemia in second remission, 27; and 25 showing immunodeficiency or other problems. The appropriate use of broad-spectrum antibiotics, Acyclovir, amethopterin, and amphotericin-B as prophylaxis reduces the infection rate considerably in the present bone marrow transplant recipients. Generally, a pattern of infection follows the three phases of transplant course. In Phase I, moderate to severe mucositis is observed, and infection by *Staphyloccocus epidermidis* and Corynebacteria species due to intravenous catheter infection (Hickman or Brovial). In Phase II, a graft versus host disease of the GI tract allows gram-negative bacteria to gain access from the damaged GI tract epithelium. The most common organism isolated was the *Pseudomonas* species. Phase III consists of interstitial pneumonia due to viral etiology, most probably cytomegalovirus. In this phase, the greatest morbidity and mortality is observed, which corresponds to the experience of others. In the present patient population, *Varicella zoster* virus infection is controlled well. Interstitial pneumonia remains a major problem and has caused considerable mortality and morbidity among bone marrow transplant recipients in this centre.

TRANSFUSION TRANSMITTED DISEASES: PROVIDING FOR A SAFE BLOOD SUPPLY, SS Bernvil, MA Carr-Greer, JV Schifano, Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

Provision of safe blood products for transfusion remains a major challenge for every transfusion service. With the advent of a specific assay 15 years ago for the hepatitis B viral antigen, a major step was accomplished. It was soon realized, however, that although the frequency of posttransfusional hepatitis B was dramatically reduced, other infectious agents were obviously taking the lead. The term non-A, non-B hepatitis was coined for the entity of hepatitis not caused by known hepatopathic viruses. Non-A, non-B hepatitis has since been responsible for more than 90% of transfusion transmitted viral hepatitis, with a 50% frequency of chronic sequelae. The retroviral scare of the 1980s taught the blood bank community new lessons on product safety. Scientific research was fueled by the urgent need for specific tests for human immune deficiency virus (HIV 1 and 2), and very sensitive and specific techniques became available within a remarkably short time. Today's standards require that every unit of blood is tested for the presence of hepatitis B surface antigen (HBsAg), HIV antibodies, and lately, even for antibodies to human T-cell leukemia virus 1 (HTLV-1). The latest offshoot is the identification of a specific virus believed to be the main if not the sole cause of blood-borne non-A, non-B hepatitis, now termed hepatitis C. By combining donor education, donor screening through interview, and disease testing of donated blood, a very high level of safety has been accomplished. There is still concern that some donors in the early phase of infection may not be detected by present tests. New assays employing polymerase chain reaction and viral inactivation techniques may be the final answer to our concerns for a safe blood supply.

HISTOPATHOLOGY OF LUNG INFECTIONS IN IMMUNOCOMPROMISED HOSTS, F Al-Dayel, Department of Pathology, King Faisal Specialist Hospital and Research Centre, Riyadh

Immunocompromised patients fall into several categories, including those with underlying malignancy, those receiving cytotoxic therapy, those with organ transplants, and increasingly encountered in the past few years, those patients with AIDS, in whom pulmonary complications are a major cause of morbidity and mortality (up to 40-50% in some studies). The development of pulmonary infection in immunocompromised patients poses a major challenge to physicians because it demands prompt diagnosis and immediate therapeutic action due to the high mortality rate. Many of these infections are caused by unusual organisms (e.g. *Pneumocystis carinii*, cytomegalovirus, fungi, atypical mycobacteria) which are not only difficult to diagnose but frequently require invasive procedures to obtain the right specimen. Finally, even if the diagnosis is made, the treatment is often potentially toxic (e.g. amphotericin B) or even impossible. Because the clinical features in these patients are usually nonspecific, a variety of invasive and noninvasive procedures are used to obtain cultural and morphological diagnosis. These include sputum examination, bronchoalveolar lavage, and lung biopsy. In this review, the diagnostic yield from the various types of pathological specimens will be compared in order to assess their relative value in the diagnosis of pulmonary infections in immunocompromised hosts.

HISTOPATHOLOGY OF INFECTED BRAIN, A Haider, Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

The central nervous system in immunocompromised patients has been found to be involved in a wide spectrum of illnesses, as indeed are most organ systems in such patients. The neuropathology in these patients is predominantly the pathology of a large variety of opportunistic infections and includes toxoplasmosis, cytomegalovirus encephalitis, PML, and cryptococcosis. Primary lymphomas are more common than secondary ones spreading from other sites. Cerebral Kaposi sarcoma is metastatic, probably from primary foci in lung. In addition to the above pathological processes, in AIDS patients other neurological syndromes appear to be caused by direct infection of the central nervous system by HIV. These syndromes include HIV encephalopathy (subacute encephalitis, AIDS dementia complex, or AIDS-related dementia), vascular myelopathy, atypical meningitis, and painful, predominantly sensory peripheral neuropathy. The former is reported with increasing frequency and localized predominantly to the white matter in which multinuclear giant cells can be found. These are considered typical for AIDS and have been shown to contain HIV particles in their cytoplasm.

BACTERIAL INFECTIONS IN COMPROMISED PATIENTS, MY Khan, King Fahad National Guard Hospital, Riyadh

This paper summarizes current knowledge on bacterial infections in compromised patients. Factors which predispose to bacterial infections include immune dysfunction, neutropenia, and certain nonspecific factors such as iatrogenic procedures, alterations in microbial flora, and anatomic barrier damage. Types of bacterial infections among compromised patients vary according to the underlying defects. In patients with AIDS who suffer from marked cellular immune dysfunction, the most commonly reported bacterial infection is tuberculosis (avium type). In patients with humoral (immune globulin) dysfunction, such as agammaglobulinemia or multiple myeloma, common bacterial pathogens include pneumococcus, meningococcus, and *H. influenzae*. Neutropenic patients suffer mainly from infections with gram-negative bacilli. With recent extensive use of Hickman-type I.V. catheters for administration of cancer chemotherapy, an increase in infections due to gram-positive bacteria (mainly staphylococcus spp) has been noted in neutropenic patients. In conclusion, bacterial infections are frequently observed in the compromised patients. Early recognition of these infections and their prompt management with appropriate antimicrobial agents have been shown to reduce morbidity and mortality among these patients.

YEAST INFECTIONS: CLINICAL MANIFESTATIONS AND ETIOLOGY, SMH Qadri, Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

Yeast infections are by far the most common fungal infections that affect man. In recent years, there has been a steady increase in the incidence of clinically significant diseases caused by opportunistic yeasts. Conditions which predispose a patient to develop such infections include the use of long-term antibacterial therapy, immunosuppressive drugs, antiinflammatory and antineoplastic agents, debilitating diseases that affect the immune system, and seriously ill or injured patients, such as those with cancer, diabetes, severe burns, or open wounds. Severity of yeast infections ranges from benign and transient to more severe, chronic, and recalcitrant. The most common clinical manifestations consists of intertriginous cutaneous and mucocutaneous localizations. However, dissemination can occur, leading to systemic disease in several organ systems such as cardiovascular, reticuloendothelial, respiratory, genitourinary, central nervous, and skeletal systems. The most common etiological agent in yeast infections is *Candida albicans*. However, other species of *Candida* have been implicated in endocarditis, fungemia, urinary tract infections, and diarrhea. Although *Cryptococcus neoformans* is usually associated with chronic meningitis, it can cause systemic disease involving almost any organ system. Other yeasts that have been isolated from clinical specimens include species of *Cryptococcus, Geotrichum, Rhodotorula*, and *Trichosporon*.

ROLE OF CHLAMYDIA AND VIRUSES IN INFECTIONS OF COMPROMISED HOSTS, MN Al-Ahdal, Biological and Medical Research Department, King Faisal Specialist Hospital and Research Centre, Riyadh

Chlamydia and viruses are obligate intracellular infectious agents that are controlled principally by cell-mediated immune responses. Only a few reports have implicated chlamydia as agents associated with increased frequency or severity of infection in the compromised host. Infants appear to be at greater risk of developing *C. trachomatis* infection than adults. Viruses are, perhaps, the most frequently encountered agents with increased infectiousness in abnormal hosts, particularly the immunocompromised. Both RNA and DNA virus groups can become opportunistic in such patients. However, those that can cause latent, persistent, or chronic infections are implicated in most cases, and in such situations the infection is usually indigenous. The most important and frequently diagnosed virus infections in compromised patients are those caused by herpes virus and hepatitis virus groups. Many reports have been published in recent years describing infections by herpes viruses in the compromised host. All members of the human-herpes virus group (herpes simplex, cytomegalovirus, Epstein-Barr virus, and varicella-zoster virus) are detected more frequently in the immunocompromised host than in normal individuals. These viruses can cause syndromes ranging from trivial or subclinical to fulminating lethal infections in patients with most, if not all, kinds of immune deficiency diseases, malignancies, organ transplants, and malnutrition. Viral hepatitis due to hepatitis B or non-A non-B viruses has been frequently described in patients with chronic liver disease and malignancies and in patients undergoing hemodialysis. It was noted that HBsAg titer rises during the course of malignancy, then drops after effective chemotherapy. Surveillance of the compromised patient is, therefore, necessary for proper management and treatment and to prevent outbreaks of virus infection in the wards or among caregivers.

MYCOBACTERIAL DISEASE IN COMPROMISED PATIENTS, SH Siddiqi, Becton Dickinson, Johnston Laboratories, Townsend, MD, U.S.A.

Myobacterium avium complex (MAC) is one of the most frequently reported opportunistic pathogens isolated from AIDS and immunocompromised patients (17 to 28%). Other mycobacterial infections in AIDS patients have also been reported. Infection due to *M. tuberculosis* varies depending on the the geographic location and prevalence of tuberculosis, ranging from 5 to over 50%. It appears that the gastrointestinal tract is the portal of entry from where the infection gets disseminated. Blood and stool are the specimens of choice. Originally blood was difficult to culture because of the lysis-centrifugation step. A new BACTEC Middlebrook 7H13 medium has been introduced recently in which 5 ml of blood sample is directly inoculated for isolation of mycobacteria. Other specimens can also be inoculated in 7H13 or in the BACTEC 12B medium for efficient and earlier detection of mycobacteria. There is no clear evidence of any difference between MAC isolated from AIDS and non-AIDS patients. Generally, serotype 4, 6, and 8 are predominant in AIDS patients but geographic variation of serotypes is known. In vitro drug susceptibility of MAC may vary significantly due to the strain variation and the method of testing. Our studies indicate more susceptibility of MAC in BACTEC 12B liquid medium as compared to the solid media. It appears that there may be a late emergence of drug resistance if drug media are incubated for longer periods. The clinical relevance of in vitro susceptibility results is yet to be investigated.

USE OF MONOCLONAL ANTIBODIES IN THE LABORATORY DIAGNOSIS OF INFECTIONS, ST Al-Sedairy, Biological and Medical Research, King Faisal Specialist Hospital and Research Centre, Riyadh

Infectious disease can be definitively diagnosed by documenting the presence of the agent known to cause the disease, by detecting a specific product of the infecting agent, or by detecting an immunologic response specific to the infecting agent.

Early diagnosis of infection and correct definition of the etiological agent are extremely important in managing severe life-threatening infections in immunocompromised patients. Most of these patients have a very late and weak immunological response, which greatly interferes with rapid diagnosis. The ability to detect a specific product of the infecting agent has not been developed to an acceptable level, so that at present documentation of the presence of the infecting agent is still the best method. Sometimes the success in growing such organisms is reduced by antibiotic treatment. One of the more promising techniques is that of infectious agent antigen detection by monoclonal antibodies. These homogeneous, highly specific agents have several advantages over more classic microbiological techniques, including rapidity, efficiency even in the face of prior antimicrobial activity, and definite proof of an etiological relationship; contamination is seldom a problem in these rapid tests. Nowadays there are many monoclonal antibody-based assays. The number is growing, and they are becoming routine assays in many microbiology laboratories.

ANTIBIOTICS AND MICROBIAL PATHOGENESIS IN THE COMPROMISED HOST, AM Shibl, King Saud University, Riyadh

Despite the availability of potent antibiotics, high mortality rates are associated with certain infections. Antimicrobial agents may have a significant bactericidal effect in vitro but the effect in vivo may sometimes be disappointing. This is especially true in immunocompromised hosts. In general, antimicrobial treatment is difficult when the immune system is not functioning adequately, and mortality attributable to infections remains high in patients with immune deficiencies. In order for microorganisms to be pathogenic they must be able to utilize the host tissue components which allow them to outgrow the host normal flora and overcome or fail to stimulate the various host defense mechanisms which would otherwise kill them. The host has evolved a battery of physical and chemical mechanisms to prevent such events. The virulence of microorganisms can be considered as a series of the following events, gaining access to host by survival on or penetration of skin and mucous membranes (i.e., adherence or attachment), in vivo multiplication, inhibition by or avoidance of the host's protective mechanisms, and production of disease or damage to the host. The antibiotics may have effects on infecting microorganisms that alter their virulence beyond simply killing them or reducing their capacity for growth. The effect of antibiotics on the virulence of microorganisms can be evaluated in several ways: by studying changes in ability to adhere to epithelial cells, by monitoring changes in toxin and enzyme (virulence factors) production, and by studying alterations in susceptibility to host defense mechanisms including chemotaxis, phagocytosis, and complement-mediated immunity. A better understanding of how antibiotics interfere with the host-parasite interaction is important because of the increasing number of compromised hosts in whom even a marginal influence on the host response may have a significant effect on the outcome of treatment.

UPDATE ON ANTIMICROBIAL AGENTS, PARTICULARLY ANTIVIRALS AND ANTIFUNGALS, ME Ellis, BK Mandal, Department of Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

The HIV pandemic has provided an unsurpassed challenge for the treatment of a vast range of opportunistic infections. This review focuses on three areas only. (1) Fungal infections, particularly cryptococcus and oropharyngeal candidiasis, are common conditions and first-line antifungal treatment often fails to effect cure or toxicity. We report the results of a study designed to test the efficacy and safety of oral fluconazole in HIV-associated oropharyngeal candidiasis. Of 21 assessible subjects, 17 were clinically cured at the end of the first treatment phase. In the maintenance phase, 7 of 9 patients were maintained free of candidiasis for 16 weeks compared with only 1 of 5 patients receiving placebo. (2) An indirect approach in the management of opportunistic infections has been to use antiretroviral strategies. Zidovudine has been the most notable advance, but toxic problems may limit its usefulness in some individuals. The triple properties of alpha 2a interferon have led to its investigation in several areas of HIV disease. The results of an open study of recombinant interferon on the clinical and immunological status of 14 HIV seropositive individuals was presented. Administration of interferon for up to 18 months was found to be safe. Skin energy, pokeweed mitogen, and phytohemagglutination responses initially improved in 6 of 7, 6 of 13, and 9 of 13 patients, respectively. Some clinical HIV disease indicators also improved, including idiopathic thrombocytopenic purpura and lymphadenopathy, but by 15 months most patients experienced significant clinical/immunological deterioration. (3) Finally, since *Pneumocystis carinii* pneumonia is a major opportunistic pathogen, some key advances in its management were summarized.

MANAGEMENT OF INFECTIONS IN IMMUNOCOMPROMISED PATIENTS, JW Hathorn, Divisions of Infectious Disease, Hematology and Oncology, Duke University Medical Center, Durham, NC, U.S.A.

The cancer patient poses a unique challenge in that disease and treatment-related aberrations of the immune response leave these individuals at increased risk to a variety of bacterial, fungal, viral, and protozoal pathogens. Of the multiplicity of factors, the severity and duration of granulocytopenia is perhaps the most important. Early retrospective studies identified the common bacterial pathogens, and underscored the high morbidity and mortality (50-75%) among granulocytopenic patients who received antibiotics only after their isolation. The value of empirical antibiotic therapy at the onset of fever in granulocytopenic patients has been well established. By necessity, early empirical regimens required a combination of antibiotics to provide: (1) an appropriately broad spectrum of activity; (2) synergistic activity of aminoglycosides and antipseudomonal penicillins against gram-negative aerobes; and (3) a reduction in the emergence of resistant pathogens. Thus, combinations of aminoglycosides with antipseudomonal penicillins and/or antistaphylococcal agents gained widespread acceptance. The advent and ability of third-generation cephalosporins, and the thienamycins, to provide broad-spectrum activity with a single drug has led to reassessment of empirical regimens. There is mounting evidence that an appropriately chosen single antibiotic (i.e., ceftazidime, cefoperazone, and imipenem-cilastatin) is as effective as a standard combination. Despite the efficacy of empirical "monotherapy," questions and controversies regarding the optimal management of febrile, granulocytopenic patients persist. For example, is combination therapy more efficacious than monotherapy for gram-negative bacteremia, especially in patients with profound, prolonged episodes of neutropenia? Should vancomycin be utilized empirically for persistently febrile, granulocytopenic patients? Additional concerns include the duration of antibiotic therapy in persistently granulocytopenic patients who have defervesced following the use of empirical antibiotics, and the role of antimicrobial prophylaxis, an issue which has "resurfaced" with the availability of quinolone antibiotics. Despite the dramatic improvement in infectious supportive care over the last two decades, a significant number of cancer patients still succumb to an infectious combination. The recent isolation, characterization, and cloning of hematopoietic colony-stimulating factors and "biological response modifiers" provide the opportunity to make further progress against these ubiquitous infectious complications. The utilization of these new products hopefully will provide the means to prevent, ameliorate, or treat more effectively established infections in these immunosuppressed patients. Of even greater significance, perhaps, is the possibility of administering more effective or more intensive chemotherapy to those patients in whom a tantalizing effective (albeit short-lived) antineoplastic response has been blunted by dose-limiting bone marrow (or immune) toxicity. As our understanding of these endogenous "immune mediators" increases, the ability to make yet another quantum leap in antineoplastic and supportive care may be at hand.

ANALYSIS OF LYMPHOCYTES SUBSET IN SAUDI POPULATION BY FLOW CYTOMETRY, ST Al-Sedairy, JC Lee, K Al Hussein, KV Sheth, GT Robert, Departments of Biological and Medical Research and Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

We examined the distribution of percentages and absolute numbers of CD3, CD4, CD8, and CD19 in normal Saudi blood donors. Some Western Caucasian donors were included for control comparison. Combinations of PE-conjugated MoAbs and FITC-conjugated MoAbs were used to characterize T-cell subsets. The two-color-labeled cells were analyzed by Becton Dickinson FACScan and the dual fluorescent subsets were discriminated by Simulset software together with a Hewlett-Packard 310 computer. The preliminary results (27 donors) show that the mean ratio of Th/Ts of Saudi was 1.5 ± 0.4 compared with 2.0 ± 0.5 of Western Caucasians. These observations support the hypothesis that Th-Ts ratios in Saudi populations are lower than those of Western Caucasians.

APPLICATION OF FLOW CYTOMETRY TO THE DIAGNOSIS OF HYDATID DISEASE, K Al-Hussein, JC Lee, ST Al-Sedairy, SMH Qadri, Departments of Biological & Medical Research and Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

This study was undertaken to establish methodology for the utilization of flow cytometry in the application of infection identification. Sera from 25 patients with hydatid disease (confirmed by radiology, endoscopy, or surgery) and highly positive IHA were collected. Normal sera and patients with low IHA titers were used as controls. An indirect immunofluorescent assay was used to study patient sera reactivity against sheep red blood cells (SRBC) sensitized with soluble purified *E. granulosus* antigen obtained from the hydatid fluid or fertile cysts from sheep (IHA kit, Behring). We also sensitized our own SRBC with larval parasite antigen crude extract. The analysis was done on a Becton Dickinson FACScan. The results showed that flow cytometry analysis is sensitive and can be used to detect very low titers of antibody in patients' sera. The results of flow cytometric analysis correlated with IHA titers. We also observed increased sensitivity when using SRBC sensitized with larval parasite antigen.

COMPARISON OF LATEX AGGLUTINATION TEST WITH CYTOTOXIC ASSAY FOR DETECTING *CLOSTRIDIUM DIFFICILE*-ASSOCIATED COLITIS IN COMPROMISED PATIENTS, SMH Qadri, J Akhter, S Ostrawski, SGM Qadri, BA Cunha, Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

Toxogenic strains of *Clostridium difficile* produce enterotoxins A and B that have been implicated in antibiotic-associated pseudomembranous enterocolitis. Detection of toxin in feces by cytotoxic assays (CTA) in cell cultures has been used as a reliable method that correlates well with the clinical disease. Since the majority of clinical laboratories lack the facilities to perform cell cultures, commercial latex agglutination (LA) assays have drawn much interest due to their simplicity, rapidity, and feasibility for use in most diagnostic laboratories. We compared the sensitivity and specificity of one LA method (Marion Labs, Kansas City, MO) with the CTA using diarrheal stool specimens from 652 patients. Specimens from 71 (10.9%) patients were found positive with CTA and 98 (15%) by LA. Of these, 67 stools were positive by both methods. Four specimens showed CTA+/LA-results. Of 31 specimens that were LA+/CTA-, 23 were obtained from leukemic bone marrow transplants, and 4 from renal transplant. Organisms included *Giardia lamblia* (3); *Salmonella enteritidis* (3); *Blastocystis hominis* (4); Rotavirus (2), and *Shigella boydii* (1). No significant organisms were found in the rest of the LA+/CTA- specimens.

DIFFERENTIAL CYTOTOXICITY OF PERIPHERAL BLOOD LYMPHOCYTES ACTIVATED IN RESPONSE TO VARIOUS CYTOKINES: IN VITRO REGULATION OF GM-CFU OF HUMAN BONE MARROW, ST Al-Sedairy, KV Sheth, RS Parhar, P Ernst, Departments of Biological and Medical Research, Pathology and Laboratory Medicine, and Bone Marrow Transplant Unit, King Faisal Specialist Hospital and Research Centre, Riyadh

The effect of various recombinant cytokines (i.e., IL-1, IL-2, IL-3, IL-4, IL-6, IFNy TNF, GM-CSF), either singly or in combination with IL-2 to induce killer cells (cytokine-induced killer cells) was investigated to evaluate the degree of killing of various human NK-sensitive K562 or NK-resistant Daudi cell lines and the differential effect on the clonogenic ability of human bone marrow to produce GM-CFU in vitro. The killer cells produced by co-culturing PBL for 3-5 days with GM-CSF, IL-1, IL-6, or IFNy had very little LAK-like activity, while IL-3, IL-4, and TNF did not generate any significant killer activity. IL-2 alone resulted in higher killer activity. Addition of IL-3 and IL-4 to IL-2-induced killer cells did not improve the LAK cell function, whereas co-culture of IL-1, IL-6, or GM-CSF with IL-2 resulted in the highest killer activity. IFNy and TNF had no significant effect on the LAK cells generated with IL-2. IL-2 alone, IL-2 + IL-1, IL-2 + IL-1 + IL-4, and IL-2 + IFNy induced LAK cells when co-cultured with human bone marrow had no inhibitory effect on GM-CFU colonies. IL-2 + GM-CSF, IL-2 + IL-6-dependent LAK cells had a stimulatory effect on GM-CFU whereas IL-2 + TNF-induced LAK cells were highly inhibitory for GM-CSF (*P*-<0.02). The results of these studies point to the importance of selecting various combinations of cytokines to carry out cytokine therapy without compromising the clinical outcome.

FINE-NEEDLE ASPIRATION BIOPSY OF RENAL ALLOGRAFTS, M Akhtar, Department of Pathology, King Faisal Specialist Hospital and Research Centre, Riyadh

The traditional method for evaluating the status of renal allografts is by performing a tissue biopsy for histological evaluation. This technique has been used for several decades with excellent results. The conventional tissue biopsy, however, has limitations because it is an invasive procedure and is certainly not without morbidity. Furthermore, tissue biopsies cannot be repeated at frequent intervals to assess the response to therapy. In recent years the use of FNAB in the evaluation of allografts is gaining increasing acceptance by pathologists as well as nephrologists. The technique has the advantage over conventional histology in that it is a minor procedure which can be easily performed in the outpatient clinic and can be repeated frequently. It is tolerated very well by the patient and has been found to be free of complications. Interpretation of these biopsies, however, requires special expertise, training, and skill. Once the technique is mastered, the usual complications in renal allografts such as cellular rejection, acute tubular necrosis, and cyclosporin toxicity can be diagnosed with confidence. Assessment of vascular rejection and chronic rejection, however, still require a tissue biopsy for definitive diagnosis. At King Faisal Specialist Hospital and Research Centre, FNAB of renal transplants was started in June 1989. A preliminary review of the results was presented and details of the method of performing, processing, and interpretation of these biopsies will be outlined.

IMMUNOGLOBULIN-DEPENDENT IN VITRO SUPPRESSION OF VARIOUS KILLER CELLS, ST Al-Sedairy, KV Sheth, RS Parhar, and P. Ernst, Departments of Biological and Medical Research, Pathology and Laboratory Medicine, and Bone Marrow Transplant Unit, King Faisal Specialist Hospital and Research Centre, Riyadh

Intravenously administered immunoglobulin (IVIG) is used in the treatment of patients with antibody deficiency syndrome, hypoglobulinemia, or agammaglobulinemia. IVIG has also been used in other clinical stituations in patients with thrombocytopenia and autoimmune neutropenia. Very little is known about the effect and mechanism of IVIG on the various alloreactive lymphocytes and other killer lineage cells; most of the studies regarding IVIG have focused only on the macrophage FC system, enhanced elimination of circulating immune complexes, enhanced platelet production, or immune modulation of T and B lymphocytes during inflammatory responses. The present study was designed to evaluate the suppressive effect of IVIG on the activation of lymphocytes, mixed lymphocyte culture, cytotoxic T-lymphocyte generation, natural killer cells, and lymphokine-activated killer cells for possible use in bone marrow transplant patients. The results of these studies were consistent with our hypothesis that IVIG down regulate the activation and generation of various killer lineage lymphocytes. At least one of the important mechanisms of action of IVIG is suppression of IL-2 receptor expression during lymphocyte activation. Taken together the results of this study have great implication in clinical transplantation.

IN VITRO SUSCEPTABILITY OF CLINICAL ISOLATES TO AXTREONAM, LE Brodie, G Lee and G Al-Okayli, Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh

Aztreonam is a novel antibiotic belonging to the class of monobactams with excellent inhibitory activity against gram-negative bacteria. We tested the in vitro activity of aztreonam against 1291 clinical isolates prior to availability of this drug in Saudi Arabia. The strains of bacteria used in this study consisted of 919 isolates of *Enterobacteriaceae*, 237 or *Pseudomonas*, 34 of the *Acinetobacter-Flavobacter* group, and 101 isolates of *Brucella melitensis*. Although all 33 isolates of *Serratia marcescens* were inhibited by aztreonam, 17% of Enterobacter-*Providencia-Morganella* and approximately 5% of *Escherichia* and of *Klebsiella* were resistant to this antibiotic. As compared with 8 to 10% resistance reported in the English literature for *P. aeruginosa*, 28% of our isolates were inhibited in vitro by aztreonam. It was less inhibitory to other pseudomonads, *Acinetobacter* and *Flavobacter*. Since the clinical isolates tested were also relatively more resistant to other antibacterial agents, the overall activity of aztreonam was found to be comparable or superior to third-generation cephalosporins and aminoglycosides.

THROMBOCYTOPENIC PURPURA TREATED WITH PLASMA EXCHANGE. A REVIEW OF NINE CONSECUTIVE CASES TREATED OVER A DECADE, SS Bernvil, AA Padmos, H Clink, KV Sheth, DG Spence, GT Roberts, JV Schifano, King Faisal Specialist Hospital and Research Centre, Riyadh

Seven female and 2 male patients (aged 13-45 years) were admitted during the last decade with peripheral blood smears indicative of microangiopathic hemolytic anemia and symptoms such as fever, jaundice, and bleeding with a history of recent or ongoing infection (7), early puerperium (2), or advanced malignancy (1). Seven patients had signs of central nervous system involvement ranging from numbness and spasms to hemiplegia. Platelet counts averaged $25/10^9/L$ (range, $5\text{-}67\times10^9/L$). Coagulation profiles were normal except in one patient who died within 2 hours of admission due to cerebral hemorrhage. Therapeutic plasma exchange was undertaken in 8 patients, using a Haemonetics or IBM/COBE 2997, removing on consecutive days a full volume of plasma (2-3 L) and replacing with a 1:1 mixture of fresh frozen plasma and saline. Patients received an average of 4 exchanges (range, 2-7). Seven patients received steroids and two patients were treated with Aspirin and Persantine. Seven patients experienced uneventful recovery while one patient remained thrombocytopenic although the red cell picture normalized during the treaatment. This patient died 3 months later of advanced bilateral cancer of the breast. Thus, in seven of nine patients admitted with the diagnosis of thrombocytopenic purpura, the clinical symptoms of microangiopathic anemia were successfully reversed after extensive therapeutic plasma exchange.

INTERNATIONAL SYMPOSIUM ON PHARMACY PRACTICE IN SAUDI ARABIA CURRENT AND FUTURE TRENDS

Organized by Department of Pharmacy Services, King Faisal
Specialist Hospital and Research Centre, Riyadh, in conjunction
with the Saudi Pharmaceutical Society
13-15 November 1989

PHARMACY: A PROFESSION IN TRANSITION, FM Eckel, School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, U.S.A.

Economic developments, political forces, demographic changes, and technological advances produce forces which result in societal changes. As we think about the implication of superconductivity, artificial intelligence, information networks, and telecommunication advances, we see the possibilities of a "cybercultural" revolution. Drugs will continue to play an essential role in the future health care system. Pharmacists, likewise, will be essential health professionals, provided they recognize society's needs and prepare themselves to provide these services. A brief review of the evolution of the professional in American society forms the basis for understanding the importance of a professional today. The contemporary societal mission for the pharmacist will be explored. Manasse has coined the term "drug misadventure" to describe the broad array of phenomena associated with negative drug experiences. Today's pharmacist is one of the few health professionals who can influence positively this public policy issue. To make it happen will require a change in pharmacy education and pharmacy practice so that pharmacists can join with other health professionals as part of a new health care team. The literature is full of reports describing both the improved quality and the cost effectiveness of active pharmacists' intervention in the drug use process. The Kingdom of Saudi Arabia is already well positioned for taking advantage of the pharmacists' contributions to improved health care. Suggestions for further developments were described.

HISTORY OF PHARMACY IN SAUDI ARABIA, A Saddique, King Khaled University Hospital, Riyadh

It is difficult to write a complete review of the history of pharmacy in Saudi Arabia, especially in the absence of any literature or references to go through, but this is an essential project, which should be carried out simply because the profession of pharmacy has taken a totally new shape and improved significantly in the past decade, making it even more difficult to catch up with its changes. The development in the pharmacy profession that took place in one decade is matching the development of the profession in other countries that took place over more than two to three decades. These achievements occurred because the country was developing from a third-world to a modern country. These changes occurred at different levels—government, retail, hospital, and education. The main source of the information was government records, personal communications, and my experience over the past ten years.

PRESENT DAY PHARMACY PRACTICE IN SAUDI ARABIA, A Bawazir, College of Pharmacy, King Saud University, Riyadh

A survey was conducted to characterize the scope of pharmaceutical services provided by various Ministry of Health hospitals. A sample of twenty-six hospitals was selected from all health regions and visited by two authors. The total number of pharmacists employed were 115, of which 19% were Saudi. Seventeen hospitals have one to four pharmacists; four hospitals have five to ten pharmacists; three hospitals have 11 to 20 pharmacists; and two hospitals have no pharmacist. Sixteen hospitals (61.5%) have a floor stock drug distribution system, three hospitals (11.5%) have a unit dose drug distribution system (UDDS), and seven hospitals (27%) have floor stock combined with partial daily or UDDS. Two hospitals have an intravenous admixture service and another two hospitals have drug information centers. Full-time clinical services were not provided by any hospital, but some aspects of clinical services, such as concurrent routine monitoring of the drug therapy of patients, were provided by a few hospitals. The quality of outpatient dispensing in most hospitals is not up to standard. The survey showed a severe deficiency in Saudi pharmacy manpower and pharmaceutical equipment in most regions. Solving these deficiencies will improve the quality of pharmaceutical services and will lead to implementation of new services. *This study was supported by King Abdulaziz City for Science and Technology, grant number AT-8-91.*

FUTURE TRENDS IN PHARMACY PRACTICE: A WORLDWIDE PERSPECTIVE, ET Herfindal, Division of Clinical Pharmacy, University of California, San Francisco, CA, U.S.A.

Attempting to predict the future is risky at best. However, by learning from our experience in the last 25 years and by analyzing current trends, it is possible to extrapolate and to make some predictions about the future of the pharmacy. By looking at current trends such as manpower statistics, economics of health care, population demographics, advances in technology, the consumer movement, role blurring, pharmacy education, specialization, and other trends, it is possible to begin to plot a scenario for the future. A number of conferences have been held to attempt to predict the future of pharmacy, such as Pharmaceuticals in the Year 2000 held by the Institute for Alternative Futures in 1982; the Project Hope Conference, entitled Pharmacy in the 21st Century, in 1985; and finally Directions for Clinical Practice in Pharmacy sponsored by the American Society of Hospital Pharmacy at Hilton Head, South Carolina, in 1985. These conferences and numerous other smaller local and regional and international conferences have helped us begin to focus on a vision of pharmacy for the future. In addition, a limited number of future research projects have attempted to develop a consensus on pharmacy in the 21st century. It is clear that pharmacy as we know it will be radically changed in the next 20 years. Educational requirements will increase, postgraduate education will become commonplace, and specialization will continue to develop with further differentiation of the pharmacists' roles. New treatment modalities, particularly biotechnologicals, will offer opportunities for pharmacists with advanced training and skills. Consumers' needs for education and information will require pharmacists to interact much more closely with patients. Drug regulation will become much more internationalized and consistent. Rationing resources will become a reality as technology accelerates faster than our ability to pay. Automation, which has been slow to infiltrate pharmacy practice, will finally begin to have a significant impact on pharmacy practice. Computers and robotics will replace many of the repetitive functions currently performed by pharmacists and technicians, and pharmacy will become increasingly recognized as a knowledge-based profession.

CURRENT RECOMMENDATIONS IN THE TREATMENT OF HYPERTENSION AND THE PHARMACIST'S ROLE, LK Jim, College of Pharmacy, King Saud University, Riyadh

Treatment of hypertension is usually lifelong. Reduction in systemic vascular resistance together with preservation of cardiac output is the optimal method of achieving blood pressure control. Initial treatment should be chosen from non-drug therapy (e.g., weight reduction, decreased sodium consumption). In choosing drug therapy, the efficacy and side effects of an agent vary in different population subsets and consideration must be given to coexisting medical diseases. ACE inhibitors, beta-blockers, calcium antagonists, and alpha$_1$-blockers all have a very low risk of causing electrolyte and metabolic disturbances and are considered first-line drugs. The cost of the drug treatment is also important, with thiazide diuretics being the cheapest and ACE inhibitors and calcium antagonists the most expensive. Thiazide diuretic agents are recommended in patients with normal renal function, blacks, and the elderly, and in those with asthma, congestive heart failure (CHF), obesity, hypercalciuria, and primary systolic hypertension. Beta blockers are used in white patients younger than 50 years old, and if coronary artery disease (CAD), migraine, anxiety, gout, or hyperthyroidism are present. ACE inhibitors can be used regardless of age, in athletes and white patients, and in patients with CHF secondary to systolic dysfunction. Calcium antagonists can be used in the elderly, blacks, and patients with CAD, peripheral vascular disease, tachycardia, gout, diabetes, or asthma. Alpha$_1$-blockers can be used in hypercholesterolemic, asthmatic, and diabetic patients as well as in athletes and those with gout.

CURRENT CONCEPTS IN DIABETES MELLITUS: TREATMENT AND PHARMACIST'S ROLE IN PATIENT EDUCATION, MA Koda-Kimble, School of Pharmacy, University of California, San Francisco, CA, U.S.A.

Diabetes mellitus is a syndrome resulting from an absolute or relative lack of insulin. There are two major clinical categories: insulin-dependent mellitus (IDDM or Type I) and non-insulin-dependent diabetes mellitus (NIDDM or Type II). In contrast to patients with IDDM, patients with NIDDM tend to be overweight and have a strong family history of diabetes. While IDDM patients are absolutely dependent on insulin therapy, the primary form of treatment for NIDDM patients is a weight-reduction diet. NIDDM patients often require oral antidiabetic agents to minimize the symptoms associated with hyperglycemia. If symptoms are not controlled, insulin therapy must be initiated. The ultimate goal in the treatment of all patients with diabetes is to make them self sufficient in the management of their disease. The development of home blood glucose monitoring and intense patient education has made it possible for some patients to achieve normoglycemia. Since many factors can influence blood glucose control (e.g., diet, exercise, drugs, and illness), patients can become easily confused about the disease and its management. Pharmacists can become vital members of the health care team involved in the treatment of the patient with diabetes by: (1) helping the patient select the proper equipment; (2) encouraging the patient to comply with therapy; and (3) educating the patient regarding the proper use of insulin, oral antidiabetic agents, and testing materials; interpretation of blood or urine glucose test results; sick-day management; and the recognition and treatment of hypoglycemia.

THE PHARMACIST AS A SOURCE OF PATIENT EDUCATION: COUNSELING TECHNIQUES, A Al-Dhewailia, College of Pharmacy, King Saud University, Riyadh

Patient noncompliance with a medication regimen is a significant problem which has both clinical and economical complications. It has been demonstrated in the literature that the pharmacist is capable of making a valuable contribution to the drug therapy of the patient. The education of patients about their medication represents an important role for pharmacists. Patient education involves counseling patients to acquire the knowledge, skills, and behavior to be responsible for compliance with a drug therapy plan. It offers an opportunity to enhance the "physician-patient-pharmacist" relationship and may be the best way to show the public and other professions that pharmacists are interested in the patient's health. A review of different educational techniques was presented.

OVERVIEW OF NEW DRUGS, J Gee, College of Pharmacy, King Saud University, Riyadh

The objective of the overview of new drugs approved by the US FDA in recent years is to identify those which significantly contribute to the pharmacotherapy of diseases. Among these new drugs, alteplase (TPA) was introduced as an alternative fibrinolytic agent. Zidovudine (AZT) was approved as the first effective antiviral agent for the treatment of HIV. Lovastatin represents a new class of enzyme inhibitors that are effective in lowering blood cholesterol levels. In the realm of antibiotics, new beta-lactams (aztreonam, imipinem) and new quinolones (norfloxacin, ciprofloxacin) have received much attention in the recent literature. Encainide was marketed as a new classic antiarrhythmic agent which does not aggravate congestive heart failure (CHF). Esmolol was added to the beta-blocker class for short-term control of supraventricular tachycardias. Lisinopril joins other ACE inhibitors for the treatment of hypertension and is being investigated for use in CHF. Nicardipine is a new calcium channel blocker which does not depress myocardial contractility. New drugs for treatment of GI diseases include famotidine, nizatidine, misoprostol, and mesalamine.

WHO's ACTIVITIES IN THE DRUG FIELD, A Wehril, World Health Organization

A brief history was given on the development of WHO's pharmaceutical program. As a follow-up on the Nairobi Conference of Experts on the Rational Use of Drugs and the ensuing

Revised Drug Strategy, WHO has been assigned new tasks which are carried out by the Pharmaceuticals Unit and the Action Programme on Essential Drugs. The latter work offers support to developing countries wishing to formulate or revise their national drug policies with particular emphasis on assuring the availability and rational use of essential drugs, particularly in primary health care. Recent publications are "National Drug Policies," "Ethical Criteria for Drug Promotion," and the "World Drug Situation." The Pharmaceuticals Unit with its normative functions is a partner to drug regulatory authorities and is responsible for stimulating (where they do not yet exist or strengthening where they are already in place) drug regulation and control structures. For this purpose, Guiding Principles for Small National Drug Regulatory Authorities and for the implementation of the Certification Scheme have been developed. Other normative and supportive activities comprise: standardization of drug nomenclature–quality assurance: International Pharmacopoeia–advice for setting up and running drug quality control laboratories—basic tests-standards for GMP–WHO Certification Scheme: drug safety and efficacy–essential drugs model list–model prescribing information–exchange of information on drug regulatory actions–adverse reaction monitoring; Publication of *WHO Drug Information*–UN list–training activities–role of the pharmacist in the health care system–CIOMS publications.

PHARMACY SERVICES AT THE UNIVERSITY OF CALIFORNIA AT SAN FRANCISCO, ET Herfindal, Division of Clinical Pharmacy, University of California, San Francisco, CA, U.S.A.

The Department of Pharmaceutical Services at UCSF has a long history of experimentation and innovation. The UCSF campus consists of the Schools of Medicine, Pharmacy, Dentistry, and Nursing and contains a medical center with a 560-bed hospital and in-patient psychiatric facility and a large ambulatory care center with multiple medical specialty clinics. Although the Department of Pharmaceutical Services is structurally under the medical center jurisdiction, the School of Pharmacy has always had a strong influence. In the middle 1960s, the relationship was solidified significantly with the joint development of an experimental decentralized unit dose system. This became known as the Ninth Floor Pilot Project and resulted in significant innovation in pharmacy practice and education that has had important impact not only in the United States but in many other countries. The department currently consists of approximately 80 staff pharmacists, faculty, residents, and fellows as well as approximately 40 pharmacy technicians and other personnel. There are four satellite pharmacies with another four in the planning stages. All IV additives, total parenteral nutrition, IV piggy-backs, and parenteral cancer chemotherapeutic agents are prepared in the central IV additive area. Staff, faculty, and residents are assigned to inpatient and outpatient services and their responsibilities include rounding with the medical teams, provision of drug and drug therapy information, monitoring of drug therapy, inservice education to nurses and physicians, obtaining medication histories, and counseling patients about their discharge medications. Pharmacists provide consultative services in total parenteral nutrition, pain management, clinical pharmacokinetics, and infectious disease. The Drug Information Analysis Service responds to patient-specific drug therapy questions from health care providers, investigates and monitors trends in adverse drug reactions, and evaluates drug requests for addition to the formulary. Pharmacists are assigned to the cardiopulmonary resuscitation team on a rotating basis. In addition to filling approximately 800 outpatient prescriptions a day, clinical services are provided in dermatology, general medicine, oncology, anticoagulation clinic, diabetic clinic, thyroid clinic, and in obstetrics and gynecology. Because of the strong integration of the pharmacy department and the School of Pharmacy, the staff and faculty of the Department of Pharmaceutical Services serve as clinical preceptors for pharmacy students on clinical rotations.

CONCEPTS IN COST CONTAINMENT: THE SAUDI EXPERIENCE, JL Lanford, Pharmacy Services, King Fahad Hospital–Saudi Arabian National Guard, Riyadh

In today's environment, pharmacists have become increasingly under pressure to control soaring pharmaceutical costs. As an example of runaway expenses, it is estimated that by the year 2000, the market for biotechnology drugs could reach $100 billion per year. The primary tools utilized by pharmacists in the 1960s and 1970s were competitive bidding and bulk discounts, which were adequate for that time. During the 1980s, drug costs have been increasing at an alarming rate with no slowdown in sight. Eight major hospital pharmacies in the Riyadh area were contacted and asked to share their experience in cost containment. Several major trends were identified upon survey of these hospitals, along with some unique ideas that were very cost effective. The major trends fell primarily under six categories: (1) generic substitution, (2) annual tenders, (3) inventory control, (4) therapeutic substitution, (5) clinical services, and (6) cooperation. Each of these areas has been successfully utilized at most of the concerned hospitals with considerable success and major cost savings. Clinical service intervention is probably the most cost effective of all methods, with a much greater impact expected in the future. The cooperation between the concerned pharmacies is excellent. It is this cooperation that plays a major role in the sharing of ideas regarding cost containment. In summary, pharmacies in Saudi Arabia have responded well to the challenge of soaring pharmaceutical costs, without compromising the quality of patient care.

COMPUTERS AND THEIR APPLICATIONS IN PHARMACY PRACTICE, M McDow, King Khaled Eye Specialist Hospital, Riyadh

Pharmacy computerization has progressed from the initial endeavors of large institutions to include a large percentage of community hospitals in the United States. Although in the past the major impetus for computerization was increased revenue and/or more efficient charge capture, with the advent of DRGs other benefits of computerization have moved to center stage. It is these advantages of automation which have formed the basis for computerization in the Kingdom. Major justifications for pharmacy automation in the Kingdom include contract compliance, increased efficiency, cost containment, and expansion of services. In most cases, hospitals in the Kingdom have not been able to contact a vendor and order a turnkey system. Due to language problems, contract requirements, and a host of other factors, pharmacy directors in the Kingdom have moved toward automation in steps. The needs of the hospital, whether financial or clinical, have been the determining factor for instituting inpatient, outpatient, or materials management programs. Justification of these expenditures has been more difficult than for a profit hospital. It is much simpler to justify a cost computer system if revenue will increase by 20%. Justification in the Kingdom rests in the areas of cost containment and clinical benefits. Nevertheless, a significant number of Kingdom hospital pharmacies have succeeded in implementing a wide variety of systems, ranging from simple P.C.-based IV additive programs to sophisticated mainframe computers encompassing the entire range of pharmacy and interdepartmental features that our colleagues in the United States have come to recognize as the norm. One such facility is our host King Faisal Specialist Hospital which has recently initiated full inpatient computerization to complement their materials management and drug information systems. Al Kharj Military Hospital has been computerized since the early 1980s and the National Guard Hospital also boasts both inpatient and outpatient systems. King Khaled Eye Specialist Hospital has long possessed materials management computerization and is in the process of developing an English/Arabic outpatient system. The long-term plan for all these and other Kingdom pharmacy departments is ultimately the goal of better patient care through continued advancement.

THE NEED FOR PHARMACY LICENSURE AND CONTINUING EDUCATION, MA Koda-Kimble, School of Pharmacy, University of California, San Francisco, CA, U.S.A.

Licensure is a process by which legal permission is given to an individual to engage in a certain occupation. In most situations, licensing is controlled by a governmental agency which services the public; theoretically, licensure assures that only proficient individuals will enter the practice. In many countries, licensure is granted to those individuals who complete education as defined by a ministry of education. In contrast, the United States has a decentralized system in which the legal authority for licensure resides with each of the 50 states and decisions regarding training and education of pharmacists reside with individual schools of pharmacy. In the U.S.A., the following are required for licensure: (1) graduation from an accredited school of pharmacy; (2) approximately 1500 hours of pharmacy practice experience; and (3) successful completion of a licensure examination. Until 1967, pharmacists in the United States could maintain their licenses simply by paying a periodic licensure fee. In the 1960s, a wave of consumerism in the United States caused the public and professionals to question whether practitioners were maintaining their competence following initial licensure. Two states instituted mandatory continuing education programs in 1967; this increased to 15 states by 1977 and to 42 states in 1989. Clearly, there is a public mandate for pharmacists to maintain their professional competency. Studies indicate that pharmacists agree. The great majority support mandatory continuing education for licensure and believe that it does indeed improve their professional competence.

THE NEED FOR A UNIFIED DRUG INFORMATION AND POISON CONTROL NETWORK IN SAUDI ARABIA, H Abou-Auda, Drug and Poison Control Information Center, College of Pharmacy, King Saud University, Riyadh

The Saudi Arabian National Drug and Poison Information Network (SAND-PIN) and its potential applications were discussed. The procedure for implementation and the contributions solicited from governmental agencies that share responsibility for the provision of health care in Saudi Arabia are outlined, based on the distribution of population and medical facilities for different regions of the Kingdom. The key component of its development is the training of personnel and the effective utilization of the available resources. In addition to providing drug information to health care professionals, the drug and poison information network is responsible for designing a new adverse drug reaction reporting system with a standard algorithm to evaluate the causality of the reported reactions. A systematic approach to developing a computerized drug and poison information database (Sau-didex) was also presented. Another proposal to link the proposed network with GULFNET (the computer network for academic and research institutions in Gulf Arab countries) was considered.

BE ALL YOU CAN BE: MAKING PHARMACY AN ADVENTURE, FM Eckel, Division of Pharmacy Practice and Division of Pharmacy Administration, University of North Carolina at Chapel Hill, Chapel Hill, NC, U.S.A.

Change can be a difficult phenomena for mankind. Yet change is the only thing certain these days. To make things happen in a changing environment requires an individual to understand his or her roots and have a defined goal. By exploring together the societal mission for pharmacy, we will gain a better perspective on our professional roots and our societal mission. Using the model of pentathlon, participants were challenged to look at their professional obligations within a framework of total societal responsibilities. Participants were challenged to develop realistic goals in each of the five areas of responsibility. Suggestions about principles of practice to guide one's professional activities were provided.

Announcements

The *Annals of Saudi Medicine* is pleased to publish announcements of educational opportunities of interest to its readers. For adequate publicity, notices of postgraduate courses, meetings, and lectures must be received at least 6 months before the date of occurrence. Please send relevant information to the *Annals of Saudi Medicine*, Publications Office, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia.

King Saud University Fellowship in Pathology

King Saud University announces the inception of a 5-year joint fellowship training program in pathology. The training will be at King Khalid University Hospital, King Faisal Specialist Hospital and Research Centre, and Riyadh Armed Forces Hospital, and is a full-time program. Application is open to interested and suitably qualified residents from all over the Kingdom. To be eligible, applicants will meet the following criteria:

1. Doctors who hold MB,BS from King Saud University or equivalent degree with at least Good grade.
2. Doctors who have finished their internship in a recognized hospital with at least a Very Good grade.
3. Successful completion of a selection examination and personal interview.
4. Applicants from other institutions should submit a letter from his/her employer that he/she will be sponsored during the whole period of training.

Applications and inquiries should be sent to the Director, Postgraduate Medical Education, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia.

King Faisal Specialist Hospital and Research Centre Postgraduate Training Programs

King Faisal Specialist Hospital and Research Centre is pleased to invite applications for the following full-time postgraduate training programs:

1. Arab Board residency training in the specialties of internal medicine, obstetrics/gynecology, pediatrics, and surgery.
2. Five-year pathology residency training program, affiliated with the Royal College of Pathologists of Australasia and the King Saud University.
3. Fellowships, both adult and pediatric, in cardiology, endocrinology, gastroenterology, infectious diseases, nephrology, hematology, and oncology. Also, adult pulmonary and critical care medicine, adult rheumatology, pediatric allergy and clinical immunology, neonatal/perinatal medicine, and pediatric neurology.

For further information contact the Director, Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia; telephone (01) 464-7272, extension 1837.

Riyadh Armed Forces Hospital, Third Annual International Course on Magnetic Resonance Imaging

The Departments of Radiology and Medical Studies of the Riyadh Armed Forces Hospital and Cleveland Clinic Education Foundation are jointly sponsoring their Third Course on Magnetic Resonance Imaging (MRI) on October 14-17, 1990. The course will provide an overview of MR technology and basic principles plus current and future applications of MR in the whole body. Participants will share in small group workshops and will have access to a large teaching file:

Faculty includes: M. Aabed (Co-ordinator), T. Bach-Gasmo,
J. Bloem, W.G. Bradley, M.N. Brant-Zawadzki,
D.C. Clark (Co-Chairman), J.V. Crues, R.
Dietrich, M. Haddad, R.E. Hendrick, R.
Herfkens, S.K. Hilal, G. Laub, R.B. Lufkin,
T. Mattsson, J. Ross (Director), J. Saaf,
H.S. Sharif (Co-Chairman), P. Sprawls, and
D. Stark.

Fee: 1,000 SR; 500 SR for Medical Staff in Training
30 hours of Category I credit will be available.

For further information contact: Department of Medical Studies, Riyadh Armed Forces Hospital, P.O. Box 7897, Riyadh 11159, Saudi Arabia. Tel: 9661 477 7714 ext. 2289/2269; fax: 9661 477 7194/477 9168.

Radiopharmaceuticals from King Faisal Specialist Hospital and Research Centre

King Faisal Specialist Hospital and Research Centre manufactures various radiopharmaceuticals at its Radionuclide and Cyclotron Operations facility with the aid of model CS-30 Cyclotron. These radiopharmaceuticals are produced according to international standards of good manufacturing practice. The Research Centre meets the high standards of quality assurance and environmental safety with regard to radiopharmaceuticals.

Radiopharmaceuticals currently produced and available for distribution throughout the Kingdom and to adjoining Arab states are as follows: thallous (Tl-201) chloride injection ($T^{1}/_{2}$ = 73 h); gallium (Ga-67) citrate injection ($T^{1}/_{2}$ = 78.3 h); iodine-123 capsules ($T^{1}/_{2}$ = 13.1 h); iodine-123 oral solution ($T^{1}/_{2}$ = 13.1 h); iodine-123 orthoiodohippurate solution ($T^{1}/_{2}$ = 13.1 h); rubidium (Rb-81) → krypton (Kr-81 m) generator ($T^{1}/_{2}$ = 4.58 h – 13 s); indium (In-111) oxine ($T^{1}/_{2}$ = 67.92 h) for cell labeling; indium (In-111) DTPA for cisternography ($T^{1}/_{2}$ = 67.92 h).

Suggestions from the medical community for additional cyclotron-produced needs are welcome.

Inquiries concerning the availability, price schedule, and technical information on specific radiopharmaceuticals should be directed to: Abbass H. Al-Marzouky, MD, Executive Director, Research Centre, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia (Fax No. 966-1-441-4839).

Joint Board for Postgraduate Medical Education Symposia

The Joint Board for Postgraduate Education is pleased to announce the following symposia for 1410-1411 (1989-1990):

1. Advances in Obstetrics & Gynaecology, Riyadh Armed Forces Hospital, 4-5 Rabi Al-Awal 1411 (23-24 September 1990).
2. Advances in Diagnostic Radiology, King Faisal Specialist Hospital and Research Centre, 11-12 Rabi Al-Awal 1411 (30 September-1 October 1990).
3. Advances in Thrombosis, King Faisal Specialist Hospital and Research Centre, 15-16 Jumada Al-Awal 1411 (2-3 December 1990).
4. 8th Annual Neurosciences, Riyadh Central Hospital, 27-28 Jumada Al-Thani 1411 (13-14 January 1991).
5. 6th Annual Paediatric Symposium, College of Medicine and King Khalid University Hospital, 26-27 Rajab 1411 (10-11 February 1991).
6. Gastroenterology and Hepatology, Security Forces Hospital, 10-11 Shaban 1411 (24-25 February 1991).
7. Postgraduate and Continuing Medical Education, College of Medicine and King Khalid University Hospital, 21-22 Shawwal 1411 (5-6 May 1991).

For further information, contact the Joint Board Office, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia; telephone (01) 467-1556 or 1564; telefax 481-1853; telex 403748 DARAYAH SJ.

King Saud University Hospitals Postgraduate Training Programs

King Saud University Hospitals (King Khalid University Hospital/King Abdul Aziz University Hospital) are pleased to invite applications for the following postgraduate training programs:

1. Arab Board residency training in the specialties of internal medicine, pediatrics, surgery, and obstetrics/gynecology.
2. Diploma courses in medical radiodiagnosis, laryngology/otology, psychiatry, and family practice.
3. Master's degree courses in pathology and family practice.
4. Residency training program in ophthalmology (in conjunction with King Khaled Eye Specialist Hospital).

For further information, contact the Director, Postgraduate Medical Education, College of Medicine, King Saud University, P. O. Box 2925, Riyadh 11461, Saudi Arabia.

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INFORMATION FOR AUTHORS

THE EDITORS of the *Annals of Saudi Medicine* welcome contributions from our readers. The *Annals* will consider for publication manuscripts of interest to readers in Saudi Arabia, the Middle East, and around the world. All submissions are subject to review by the Editorial Board and by referees in appropriate specialties.

Submission of Manuscripts. Manuscripts are received with the understanding that they are not under simultaneous consideration by another publication. An abstract published prior to a full report is not regarded as a duplicate publication. The author's transmittal letter must accompany the manuscript and contain these statements: "The manuscript has been seen and approved by all authors involved and is neither being published nor being considered for publication elsewhere. The authors transfer copyright to the *Annals of Saudi Medicine.*" Accepted manuscripts may not be published elsewhere without *Annals'* permission.

Manuscript Preparation. The format of the *Annals of Saudi Medicine* complies with "Uniform Requirements for Manuscripts Submitted to Biomedical Journals," published by the International Committee of Medical Journal Editors in Vancouver, British Columbia, in 1979 (the widely accepted "Vancouver style"), as described in the *Annals of Internal Medicine* (1982; 96 [pt 1]: 766-71). With the exception of blood pressure, all units of measurement and laboratory values must be expressed in SI units; conventional units may be included parenthetically. Authors are referred to *Annals of Internal Medicine* (1987;106[1]:114-29) for guidance in the use of SI units. Manuscripts, including tables, references, and figure legends, must be typewritten, double-spaced, on $8^1/2$ × 11 inch (21.5 × 28 cm) or size A4 paper, with margins of at least 1 inch (2.5 cm). Pages should be numbered consecutively, beginning with the title page and continuing through the last page of typewritten material. One original and two photocopies of the entire manuscript should be submitted, along with three sets of photographs.

Title Page. The title page must contain (1) title of the article, (2) correct names of each author plus highest academic degree for each, (3) each author's official academic and/or clinical title and affiliation, (4) name and address of the institution(s), (5) name and address of author to whom correspondence should be sent, if it differs from the first author, and (6) any disclaimers. For case reports, it is recommended that the number of authors be limited to four. Acknowledgment of support should be included in the Acknowledgment section at the end of the article.

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Manuscript Format. Most original articles have the following format: Introduction (the question the paper intends to answer); Materials and Methods (the study design and methods, definitions such as for diagnostic criteria, the population or patient samples, and laboratory and statistical methods); Results (the pertinent findings in a logical sequence with tables and figures as necessary); and Discussion (conclusions based on the findings, evidence from the literature that supports the conclusions, conflicting evidence, applicability of the conclusions, and implications for future research or clinical applications). Authors might consult recent issues of the *Annals* for examples of appropriate format.

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amoxycillin

Prescribing Information

AMOXIL is a broad spectrum antibiotic suitable for a wide range of infections caused by susceptible organisms.

Indications
Respiratory, ear, nose and throat, genito-urinary and skin and soft tissue infections.

Dosage
Children: Oral and injectable – up to 2 years: 62.5mg–125mg every 8 hours. 2–10 years: 125mg–250mg every 8 hours. Based on bodyweight (including neonates) 35–100mg/kg/day.
Adults: Oral – 250–500mg every 8 hours. Injectable – I.M. 250–500mg every 8 hours or more frequently if necessary. I.V. 500mg–2g every 4–6 hours. (Doses in excess of 1g should be given by infusion over 30 minutes.)

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Syrup: 125mg amoxycillin* per 5ml.
Syrup Forte: 250mg amoxycillin* per 5ml.
Paediatric drops: 125mg amoxycillin* per 1.25ml in bottles with calibrated dropper.
Injection: Vials containing 250mg or 500mg amoxycillin as the sodium salt.

*as the trihydrate.

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Contra-indications
Penicillin hypersensitivity.

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Side-effects, as with other penicillins, are usually of a mild and transitory nature; they may include diarrhoea, indigestion or an occasional rash, which may be either urticarial or erythematous: in either case it is advisable to discontinue treatment.

Further information is available from

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مساعدتا التحرير:

فرجينيا جي كروزير
شيرلي موفيت

المدونات الطبية السعودية مجلة تنشر بموجب الأمر الملكي السامي رقم ٥/م/٢٤٢٢٣ بتاريخ ١٤ شوال عام ١٤٠٠هـ. وتصدر مرة كل شهرين، وهي مشروع مشترك بين كل من كلية الطب ومستشفى الملك خالد الجامعي ـ جامعة الملك سعود، صندوق بريد ٢٩٢٥ ـ الرياض ١١٤٦١، المملكة العربية السعودية، ومستشفى الملك فيصل التخصصي ومركز الأبحاث، صندوق بريد ٣٣٥٤ ـ الرياض ١١٢١١، المملكة العربية السعودية. يتم صف وطبع المجلة بمطابع جامعة الملك سعود. يتم توزيع المدوَّنات بواسطة قسم البريد التابع لإدارة الخدمات الإدارية بمستشفى الملك فيصل التخصصي ومركز الأبحاث. كما يتولى قسم الترجمة في هذه الإدارة إعداد الملخصات العربية بالاشتراك مع الدكتور محمد زهير القاوي. كل المراسلات والاستفسارات وطرق الحصول على المستلات ترسل إلى مكتب المطبوعات على العنوان التالي:

مكتب المطبوعات
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ص.ب ٣٣٥٤
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منـدوب الاعلانـات
بي آر سي المتحدة
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الآراء التي ترد في المقالات المنشورة تعبر عن رأي أصحابها فقط ولا تعبر عن وجهة نظر مجلة المدونات الطبية السعودية. لا يسمح بإعادة طبع أي جزء من المجلة أو نسخه بأي شكل وبأي وسيلة سواء أكانت إليكترونية أو آلية، بما في ذلك التصوير والتسجيل أو الإدخال في أي نظام حفظ أو استعادة معلومات إليكتروني، بدون الحصول على موافقة مسبقة من إدارة المجلة.

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1. Proceedings of Int. Symp. Excerpta Medica 1984, 54-67.
2. Roy. Soc. Med. Int. Cong. and Symp. Series **80**, 173-180.

PRESCRIBING INFORMATION

Presentation BACTROBAN ointment: mupirocin 2% w/w in polyethylene glycol base. 15g tubes.
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Indications Bacterial skin infections, eg impetigo, folliculitis and furunculosis.
Dosage and Administration Adults and children: BACTROBAN should be applied to the affected area up to three times daily, for up to 10 days.
Precautions Avoid contact of BACTROBAN ointment with the eyes. Use BACTROBAN with caution in patients with moderate or severe renal impairment.
Use in Pregnancy There is inadequate evidence of safety to recommend the use of BACTROBAN during pregnancy.
Contra-indications Hypersensitivity to BACTROBAN or other ointments containing polyethylene glycols. This BACTROBAN formulation is not suitable for ophthalmic or intra-nasal use.
Side-effects Some minor localised effects such as burning, stinging and itching have been reported.
Storage BACTROBAN should be stored at room temperature (below 25°C).
Further information is available on request. BACTROBAN is a trademark.

International Division 001/34/2/7/89

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ANNALS
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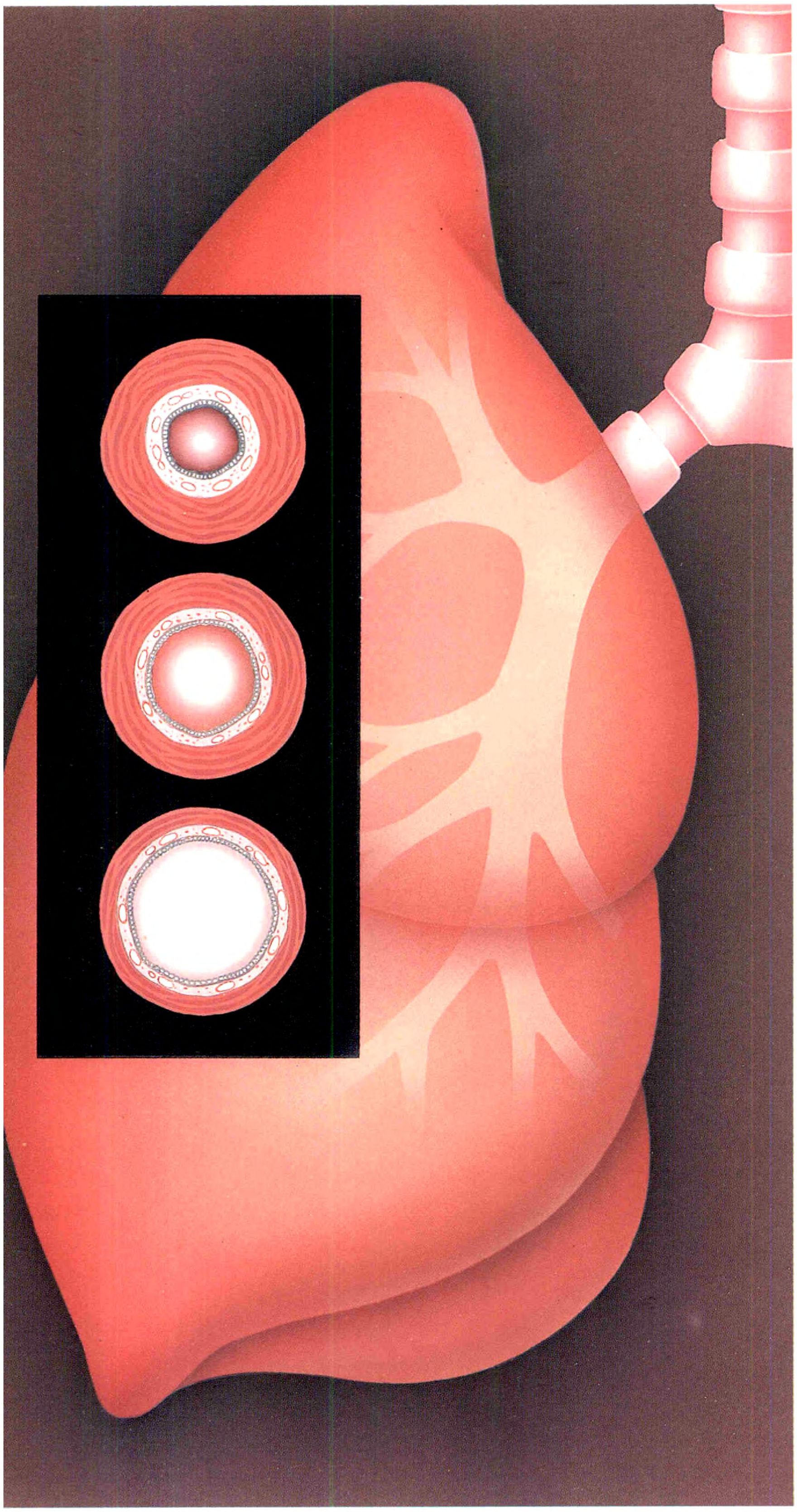
THE FIRST INHALED ANTICHOLINERGIC BRONCHODILATOR



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1. Gold W Postgrad Med J 1975:51 (Suppl 7)
2. Nadel JA New Dimensions in the Management of Airways Disease and Rhinitis. Auckland: ADIS Press 1982.
3. Tashkin DP. Am J Med 1986:81 (Suppl 5A) 81-90
4. MacVicar J et al. New Dimensions in the Management of Airways disease and Rhinitis. Auckland: ADIS Press 1982.

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and Current Awareness in Biological Sciences.
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ANNALS OF SAUDI MEDICINE

Aims and Scope

The *Annals of Saudi Medicine* is a joint project of the King Faisal Specialist Hospital and Research Centre and the King Saud University College of Medicine and King Khalid University Hospital. The journal is typeset and printed at the King Saud University Press, Riyadh, Saudi Arabia. Since July 1985, the *Annals* has incorporated *The King Faisal Specialist Hospital Medical Journal*, established in 1980.

The *Annals* is a bimonthly multidisciplinary medical journal. High-quality papers, written in English, dealing with aspects of clinical, academic or investigative medicine or research will be welcome. Emphasis is placed on matters relating to medicine in Saudi Arabia in particular, and the Middle East in general, though articles are welcome from anywhere in the world, and the *Annals* has worldwide readership.

The *Annals* publishes original articles, case reports, letters to the editor, editorials, and from time to time, special communications, commentaries, and review articles. Abstracts of meetings and symposia sponsored by the Joint Board for Postgraduate Medical Education of Saudi Arabia are published, and the proceedings of such symposia may be published if the Editorial Board considers them appropriate and relevant. The Editorial Board wishes to minimize delay between manuscript submission, decision, and publication, and accordingly authors are requested to follow carefully the instructions set out under "Information for Authors."

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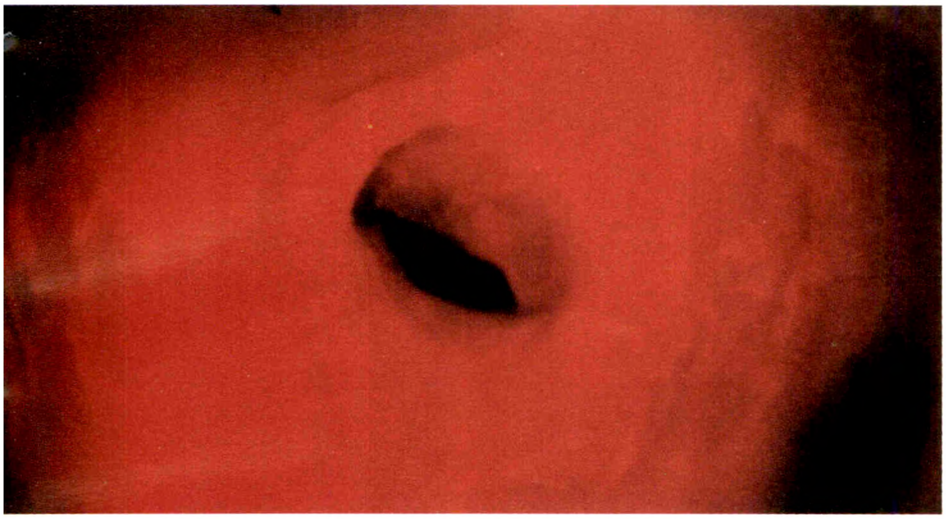
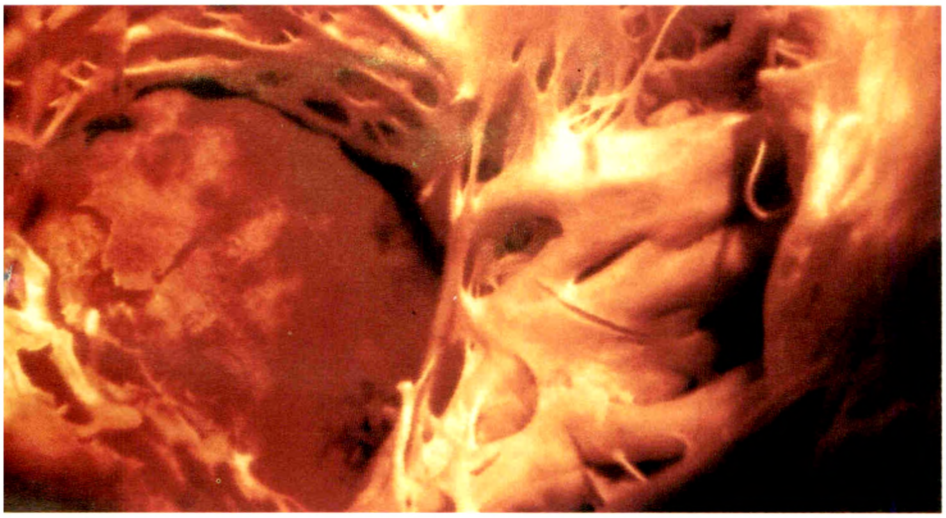
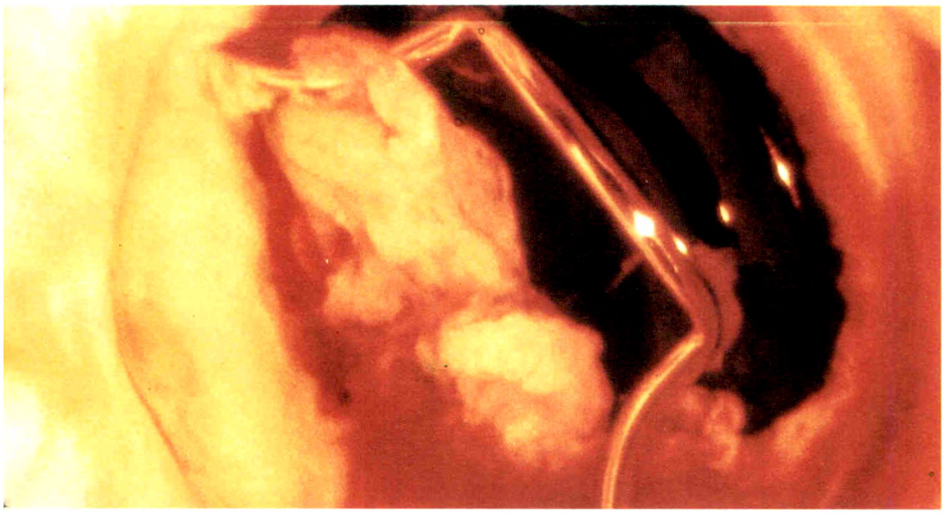
WHEN THROMBOSIS THREATENS



Thrombus in the apical part of the heart situated close to infarcted areas of myocardium. Patient 62 year old male, heavy smoker since age of 19, overweight, having work related stress who died suddenly 6 weeks after release from ICU.



Severe atherosclerotic changes in the aorta, thrombotic masses partially occluding the vessel.



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- CABG surgery
- Prosthetic cardiac valve replacements
- Cerebrovascular diseases
- Peripheral vascular diseases
- Renal diseases

1. Sharma S and Seth H. Brit. Heart Jour 1978, 40:520-529
2. Mehta J and Mehta P. Am J Cardiol 1981, 48:366-373
3. Masel B et al. Headache 1980, 20:13-18

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PRESCRIBING INFORMATION – INDICATIONS – Osteoarthritis, rheumatoid arthritis and similar conditions requiring anti-inflammatory treatment. DOSAGE AND ADMINISTRATION – **Adults:** The recommended daily dose is two tablets (1g) taken as a single dose at bedtime. For severe or persistent symptoms, or during acute exacerbation, an additional one or two tablets (500mg–1g) may be given as a morning dose. **Use in elderly patients:** In common with many drugs, blood levels may be higher in elderly patients. The recommended daily dose of 1g should not be exceeded in this age group and in some cases 500mg may give satisfactory relief. **Use in children:** There are no clinical data to recommend the use of RELIFEX in children. RELIFEX tablets should be swallowed whole without chewing. **Use in patients with impaired renal function:** See Package Insert Leaflet. PRECAUTIONS – Patients with established aspirin hypersensitivity may react in a similar manner to nabumetone. Patients with a history of peptic ulceration should be regularly reviewed for recurrence of symptoms. Fluctuations in some parameters of liver function, particularly alkaline phosphatase.

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nabumetone

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observed in patients with chronic inflam-
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lceration, severe hepatic impairment (e.g.
umetone hypersensitivity. SIDE EFFECTS –
clude diarrhoea, dyspepsia, nausea,
abdominal pain, flatulence, headache, dizziness, pruritus, rash and sedation. In clinical trials, increases in dose above 1g did not lead to an increase in the incidence of side effects. AVAILABILITY – RELIFEX tablets: Red, film coated tablets marked RELIFEX on one side and 500 on the other side. Each tablet contains 500mg nabumetone.

REFERENCES: 1. Roth SH, *Am J Med* 1987; **83** (Suppl 4B): 25–30. 2. Appelrouth DJ *et al*, *Am J Med* 1987; **83** (Suppl 4B): 78–81. 3. Carle WK, Rotman H, *R Soc Med Int Congr Symp Ser* 1985; (69): 139–148. 4. Brobyn RD, *Am J Med* 1987; **83** (Suppl 4B): 50–54.

RELIFEX is a product of research from Beecham Pharmaceuticals, Brentford, England. Further information is available from the company on request.

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the treatment
it deserves.

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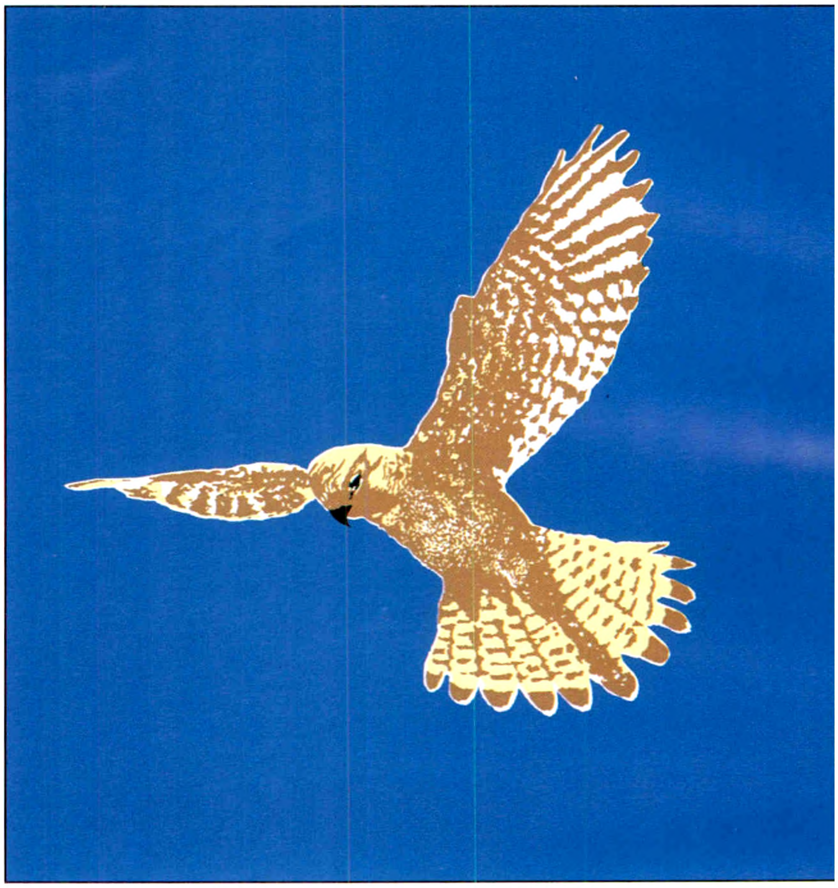

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Dosage: Oral: adults and children over 12 years: 1 tablet or 10 ml syrup morning and evening; in refractory cases up to 6 tablets or 60 ml syrup per day. Children up to 1 year: 1–2.5 ml syrup; 1–3 years: 2.5–5 ml; 3–6 years: 5 ml; 6–12 years: 7.5 ml syrup or ½–1 tablet before breakfast and at bedtime.
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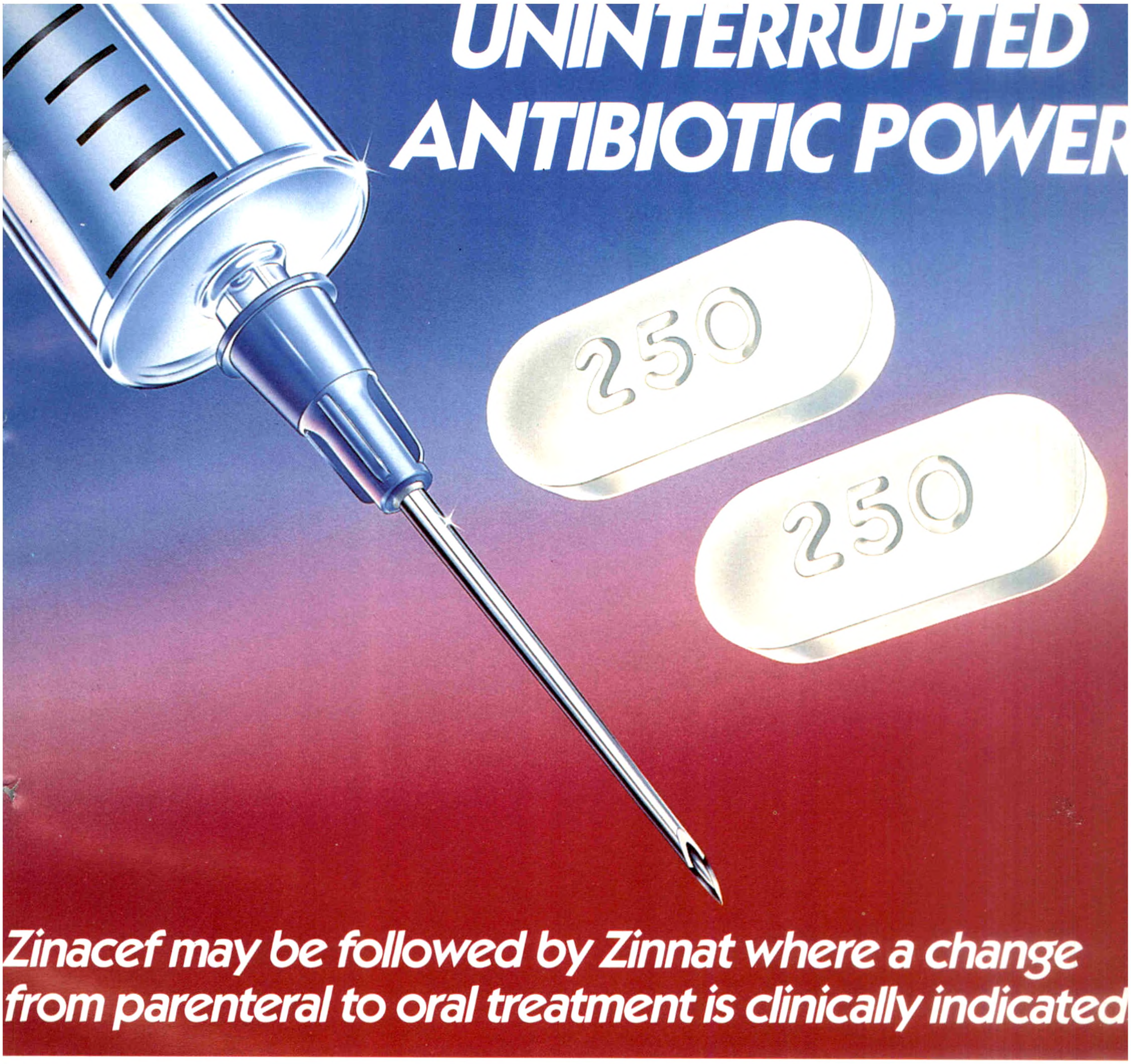

UNINTERRUPTED
ANTIBIOTIC POWER
250
250
Zinacef may be followed by Zinnat where a change from parenteral to oral treatment is clinically indicated

ZINACEF

cefuroxime

FOR DECISIVE PARENTERAL EFFECT

INACEF ABBREVIATED PRESCRIBING INFORMATION

osage: *Adults:* Generally 750mg t.i.d.i.m. or i.v. Severe infections 1.5g t.i.d.i.v. Frequency of injections can be increased 6-hourly if necessary. *Infants and children:* 30 to 100mg/kg/day in 3 or 4 divided doses. 60mg/kg/day will be appropriate r most infections. *Neonates:* 30 to 100mg/kg/day in 2 or 3 divided doses. *Gonorrhoea:* Single dose of 1.5g (2 x 750mg into ifferent sites). *Prophylaxis:* The usual dose of 1.5g i.v. with induction of anaesthesia for abdominal, pelvic and orthopaedic perations, may be supplemented with two 750mg i.m. doses 8 and 16 hours later. In cardiac, pulmonary, oesophageal and ascular operations, the usual dose is 1.5g i.v. with induction of anaesthesia continuing with 750mg i.m. t.i.d. for a further 4 to 48 hours. In total joint replacement, 1.5g cefuroxime powder may be mixed dry with each pack of methyl methacrylate ement polymer before adding the liquid monomer. **Contra-indication:** Hypersensitivity to cephalosporins. **recautions:** Cephalosporins may, in general, be given safely to patients who are hypersensitive to penicillins. Care is icated in patients who have experienced an anaphylactic reaction to penicillin. As with all drugs, Zinacef should be dministered with caution during the early months of pregnancy. Zinacef should not be mixed in the syringe with minoglycoside antibiotics. Reduce dosage when renal function is markedly impaired. (See data sheet for details.) ephalosporins at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics uch as frusemide, as these combinations are suspected of adversely affecting renal function. Clinical experience with inacef has shown that this is not likely to be a problem at the recommended dose levels. **Side effects:** Adverse reactions are are and generally mild and transient, e.g., hypersensitivity reactions (rashes and rarely anaphylaxis), gastro-intestinal isturbances, decreased haemoglobin concentration, eosinophilia, leucopenia, neutropenia and a positive Coombs' test. ransient rises in serum liver enzymes. Transient pain after i.m. injection. As with other antibiotics, prolonged use may result the overgrowth of non-susceptible organisms, e.g. Candida. **Package quantities:** Zinacef 250mg or Zinacef 750mg (for se by intramuscular or intravenous injection) in packs of 5. Zinacef 1.5g (for use by intravenous injection), packed singly. inacef 1.5g infusion packs (for use by intravenous infusion), packed singly.

innat and Zinacef are trademarks

ZINNAT

cefuroxime axetil

FOR RELIABLE ORAL POWER

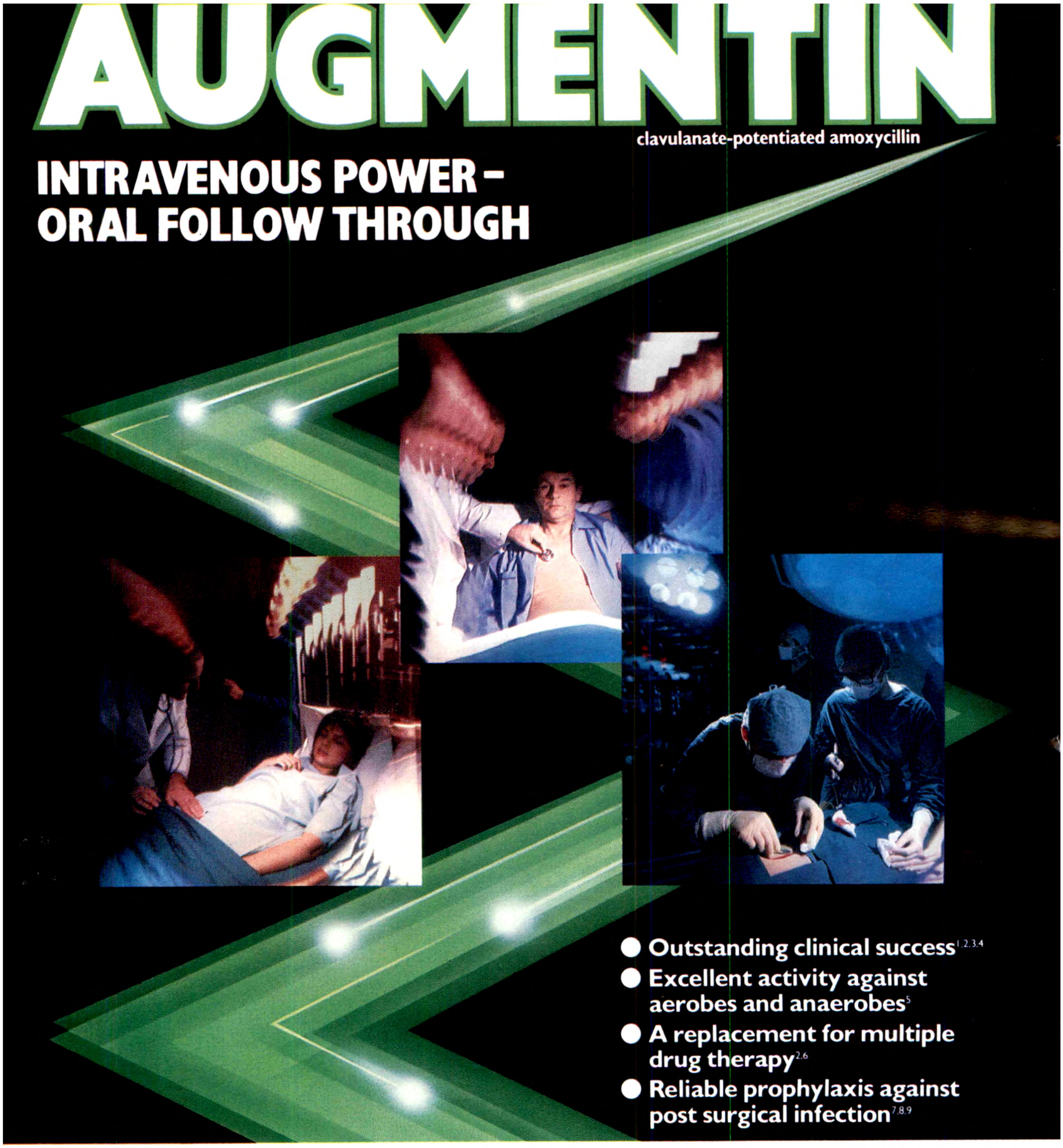
ZINNAT ABBREVIATED PRESCRIBING INFORMATION

Uses ZINNAT is indicated for infections of lower respiratory tract, ear, nose and throat, urinary tract, skin and soft tissu **Presentation** White tablets containing 125mg, 250mg and 500mg cefuroxime as cefuroxime axetil. **Dosage** *Adults:* Mo infections – 250mg twice daily. Lower respiratory tract infection – 250mg twice daily, Pneumonia – 500mg twice dail Urinary tract infection – 125mg twice daily, Pyelonephritis – 250mg twice daily. Uncomplicated gonorrhoea – 1g sing dose. *Children:* Most infections – 125mg twice daily. Otitis media – 250mg twice daily. Tablets should not be chewed crushed and therefore are not suitable for children under five years of age. ZINNAT should be taken after food for optimu absorption. **Contra-indications** Hypersensitivity to cephalosporin antibiotics. **Precautions** ZINNAT may in general be give safely to patients who are hypersensitive to penicillins, although cross-reactions have been reported with som cephalosporins and special care is indicated in patients who have experienced anaphylactic reaction to penicillin Cefuroxime axetil should be administered with caution during early months of pregnancy. **Side effects** Gastrointestin disturbances including diarrhoea, nausea and vomiting have been reported, these are generally mild and transient in natur As with all broad spectrum antibiotics, there have been rare reports of pseudomembranous colitis. Rarely, hypersensitivit reactions, eosinophilia, and transient increases of hepatic enzyme levels have been noted. **Package quantities** All strengths tablets are supplied in foil strips in packs of 10, 14 and 50. (Not all tablet strengths or pack sizes are available in every country.

WORLD CLASS ANTIBIOTICS

Glaxo

For full prescribing information for Zinacef or Zinnat, see data sheet, or contact:
Glaxomed Limited, International House, 7 High Street, Ealing,
London W5 5DB, England.


AUGMENTIN
clavulanate-potentiated amoxycillin
INTRAVENOUS POWER –
ORAL FOLLOW THROUGH
● Outstanding clinical success[1,2,3,4]
● Excellent activity against aerobes and anaerobes[5]
● A replacement for multiple drug therapy[2,6]
● Reliable prophylaxis against post surgical infection[7,8,9]

References 1. Excerpta Medica, **CCP4**, (1983), 207. 2. J. Antimicrob. Chemother., (1982) **10**, (1), 67. 3. Proc. 4th Mediterr. Congr. Chemother. Rhodes, (1985), **4**, (2 suppl.): 199. 4. Excerpta Medica, **ICS 544**, (1980), 277. 5. Ibid. (1980), 173. 6. Med. Int. (1983), (Suppl: Readings in Infections), 2. 7. Proc. 4th Mediterr. Congr. Chemother. Rhodes, (1985), **4**, (2 Suppl.), 776. 8. Br. J. Surg., (1985), **72**, (7), 571. 9. Proc. 26th ICAAC New Orleans, (1986), Abstr. 472.

Prescribing Information

Indications: Upper/lower respiratory tract infections: sinusitis, tonsillitis, otitis media, acute and chronic bronchitis, pneumonia, empyema, lung abscess. Skin and soft tissue infections: Boils/abscesses, cellulitis, wound infections, intra-abdominal sepsis. Genito-urinary tract infections: cystitis, urethritis, pyelonephritis, septic abortion, pelvic infections, chancroid, gonorrhoea. Osteomyelitis, septicaemia, peritonitis, surgical prophylaxis.

Oral dosage: Adults and children over 12 years: One tablet tds. Children 7-12 years: 10ml of 156mg syrup. Children 2-7 years: 5ml of 156mg syrup. Children 9 months-2 years: 2.5ml of 156mg syrup. Children below 9 months: No suitable presentation currently available. In severe infections the dosage may be doubled.

Intravenous dosage: Adults and children over 12 years 1.2g 6-8 hourly. Children 3 months-12 years 30mg/kg 6-8 hourly. Children below 3 months see pack insert leaflet. Surgical prophylaxis: Adults: 1.2g at induction of anaesthesia. Procedures longer than 1 hour require subsequent doses (up to 4 in 24 hours). Treatment with AUGMENTIN should not be extended beyond 14 days without review.

Contra-indication: Penicillin hypersensitivity. **Precautions:** A number of studies at high dosages have shown AUGMENTIN to be free from teratogenicity in animals; however its safety in human pregnancy has not yet been established. There is no experience of AUGMENTIN I.V. in human pregnancy therefore its use in pregnancy cannot be recommended. Changes in liver function tests have been observed in some patients receiving intravenous AUGMENTIN. The clinical significance of these changes is uncertain but AUGMENTIN should be used with care in patients with evidence of severe hepatic dysfunction. Dosage for patients with moderate or severe renal impairment should be adjusted as described in the pack insert leaflet. **Side-effects:** Uncommon, mainly mild and transitory eg. diarrhoea, indigestion, nausea, vomiting, candidiasis. If gastro-intestinal side-effects occur with oral therapy they may be reduced by taking AUGMENTIN at the start of meals. In the event of an urticarial or morbilliform rash discontinue treatment. Phlebitis at the site of injection has been reported.

Availability: 375mg AUGMENTIN tablets containing 250mg amoxycillin/125mg clavulanic acid. 156.25mg AUGMENTIN syrup each 5ml containing 125mg amoxycillin/31.25mg clavulanic acid. 600mg AUGMENTIN intravenous vials each containing 500mg amoxycillin/100mg clavulanic acid. 1.2g AUGMENTIN intravenous vials each containing 1g amoxycillin/200mg clavulanic acid. Not all presentations are available in every country.

Storage and Stability: See pack insert leaflet.

Further information is available on request.
AUGMENTIN is a product of research from
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ANNALS OF SAUDI MEDICINE

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Confidence

WHEN IMPAIRED HOST DEFENCES PUT PATIENTS AT RISK

Most hospitalised patients are to some degree immunocompromised and are therefore at special risk of infection.

Minor

- old age
- poor nutrition
- neonate
- catheters

Moderate

- surgery
- chronic debilitating diseases
- intensive care

Severe

- malignant disease
- prolonged neutropenia
- burns with loss of plasma

Infection in these patients should be dealt with decisively.

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Presentation: Fortum for injection is supplied in vials containing 250 mg, 500 mg, 1 g and 2 g ceftazidime (as pentahydrate) with sodium carbonate. **Uses**: Fortum is a bactericidal cephalosporin in antibiotic which is resistant to most beta-lactamases and is active against a wide range of Gram-positive and Gram-negative bacteria. It is indicated for the treatment of single infections and for mixed infections caused by two or more susceptible organisms. Fortum, because of its broad antibacterial spectrum, may be used alone as first choice drug, pending sensitivity test results. **Dosage and administration**: *Adults*: 1 g to 6 g i.m. or i.v. per day and by the i.p. route 125 to 250 mg per two litres of dialysis fluid (see Data Sheet for details). *Neonates, Infants and Children*: Up to two months: 25 to 60 mg/kg/day given as two divided doses has proved to be effective. In the neonate the serum half-life of ceftazidime can be three to four times that in adults. Over two months: 30 to 100 mg/kg/day given as two or three divided doses (see Data Sheet for details). In Impaired Renal Function: the dosage of ceftazidime should be reduced when the glomerular filtration rate (GFR) falls below 50 ml/min. An initial loading dose of 1 g may be given to patients with suspected renal insufficiency (see Data Sheet for details). **Contra-indication**: Fortum is contra-indicated in patients with known hypersensitivity to cephalosporin antibiotics. **Precautions**: Cephalosporins may, in general, be given safely to patients who are hypersensitive to penicillins. Care is indicated in patients who have experienced an anaphylactic reaction to penicillin. Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with nephrotoxic drugs. Clinical experience with Fortum has shown that this is not likely to be a problem at the recommended dose levels. As with all drugs, Fortum should be administered with caution during the early months of pregnancy and in early infancy. Fortum is excreted in human milk in low concentrations. Fortum does not interfere with enzyme-based tests for glycosuria. Slight interference with copper reduction methods may be observed. Fortum does not interfere in the alkaline picrate assay for creatinine. Fortum and aminoglycosides should not be mixed in the same giving set or syringe. As with other broad spectrum antibiotics, prolonged use of Fortum may result in the overgrowth of non-susceptible organisms (e.g., Candida, Enterococci) which may require interruption of treatment or adoption of appropriate measures. **Side effects**: Fortum is generally well tolerated with only infrequent adverse reactions, e.g. pain and/or inflammation after i.m. administration and phlebitis and/or thrombophlebitis after i.v. administration, rashes, fever, pruritus, anaphylaxis, gastrointestinal disturbances, headache, dizziness, paraesthesia and bad taste. Transient changes in laboratory values may occur including: eosinophilia, a positive Coombs' test, thrombocytosis, leucopenia, thrombocytopenia and slight rises in hepatic enzymes.

For full prescribing information see data sheet or contact: **Glaxomed Limited**, International House, 7 High Street, Ealing, London W5 5DR, England

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Aliment pour nourrissons
de faible poids de naissance
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مستحضر للأطفال ذوي الوزن المنخفض لدى الولادة
NESTLÉ
Net weight 400 g

Breast milk is the best food for infants, but low-birthweight infants, and particularly very low-birthweight infants, have special needs which may necessitate supplementation or, in extreme cases, even substitution of breast milk.

PRE-NAN is a special infant formula accurately adjusted to safely meet the needs of the low-birthweight infant. For normal enteral feeding or by naso-gastric tube, from the first days of life until a bodyweight of 4 to 5 kg is achieved.

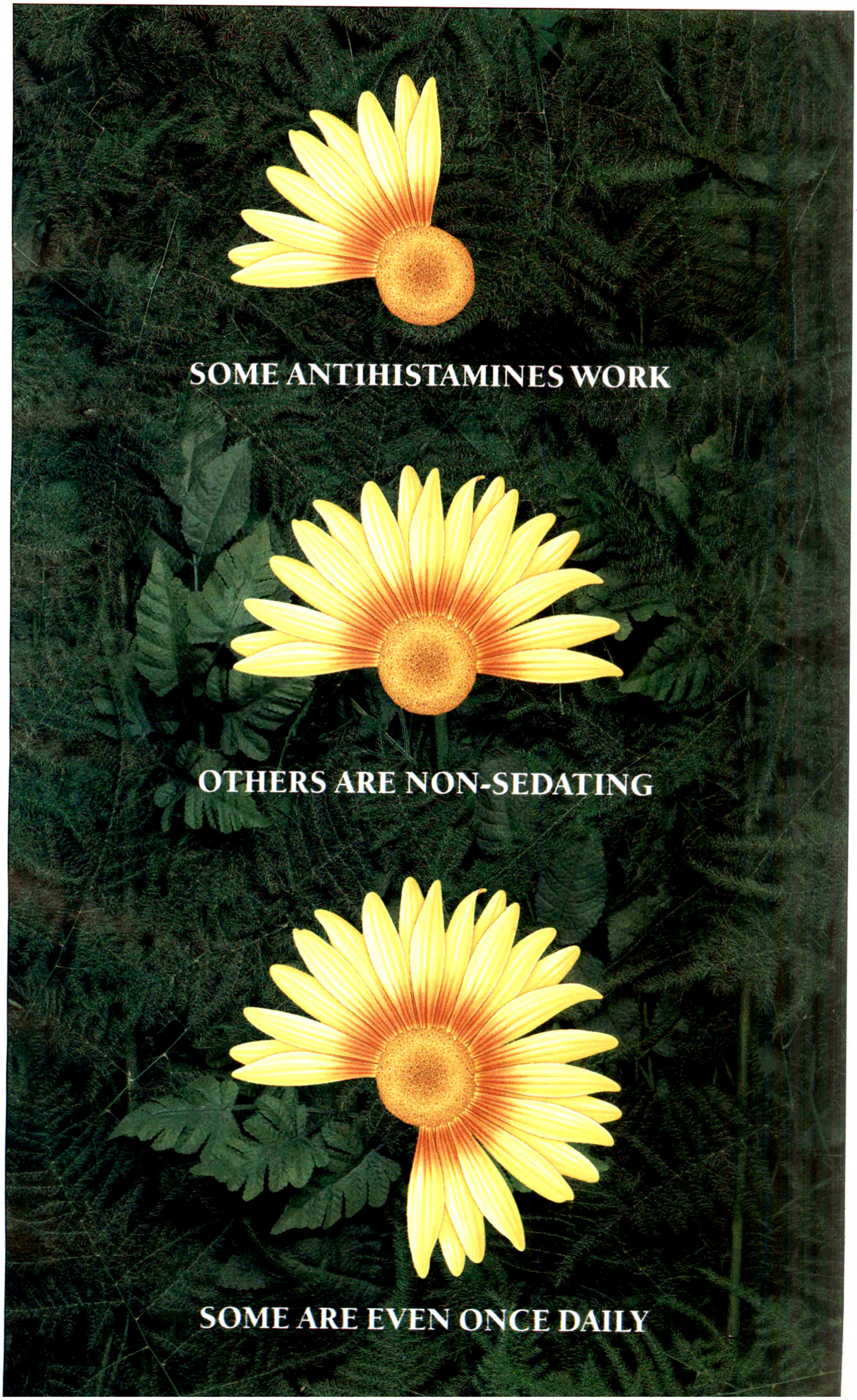
Refer to product literature for a full description of PRE-NAN and its use.

IMPORTANT NOTICE The World Health Organization (WHO*) has recommended that pregnant women and new mothers be informed of the benefits and superiority of breastfeeding – in particular the fact that it provides the best nutrition and protection from illness for babies. Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle-feeding or other foods and drinks should be discouraged since it will have a negative effect on breast-feeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breast-feed.

For most low birthweight infants the mother should be encouraged to express her breast-milk to feed her baby, if direct breast feeding is impossible. If breast-milk is not available, or must be supplemented, a special formula adapted to the specific nutritional needs of low birthweight infants should be used under strict medical control.

Continued use of a special formula should be assessed case by case in relation to the baby's progress, and bearing in mind any social and financial implications for the family. For example, if a baby is exclusively bottle-fed, more than one can (450 g) per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breast-milk is not only the best, but also the most economical food for babies. If a decision to use an infant formula is taken, it is important to give instruction on correct preparation methods, emphasizing that unboiled water, unboiled bottles or incorrect dilution can all lead to illness.

* See: International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981.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LOW PHOSPHATE INFANT FORMULA

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NESTLÉ
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- stool pH similar to breast-fed infants
- predominance of BIFIDUS bacteria in intestinal flora
- optimal bone mineralisation
- excellent tolerance and digestibility.

IMPORTANT NOTICE The World Health Organisation (WHO*) has recommended that pregnant women and new mothers be informed of the benefits and superiority of breastfeeding – in particular the fact that it provides the best nutrition and protection from illness for babies.

Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle-feeding or other foods and drinks should be discouraged since it will have a negative effect on breastfeeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breast-feed.

Before advising a mother to use an infant formula, she should be advised of the social and financial implications of her decision: for example, if a baby is exclusively bottle-fed, more than one can (450 g) per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breast-milk is not only the best, but also the most economical food for babies.

If a decision to use an infant formula is taken, it is important to give instruction on correct preparation methods, emphasizing that unboiled water, unboiled bottles or incorrect dilution can all lead to illness.

* See International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981.

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LORATADINE

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Editorial

NEW VIRAL DISEASES AND MEDICAL RESEARCH

For centuries, mankind has been plagued by infectious disorders caused by a variety of pathogens—viruses, *Chlamydia, Rickettsia,* bacteria, fungi, parasites. The immune systems of man and other animals have evolved to deal with and defend the host against such foreign intruders, but the medical literature has been witness to the constant succession of new and evolving infectious diseases appearing throughout the world. Some diseases are new while others exhibit changing patterns in clinical manifestations, morbidity, and outcome—all requiring constant vigilance and efforts on the part of the medical community to combat these new threats to the human immune system. Advances in research and technology have led to the eradication of many infectious agents, with viruses such as smallpox made virtually extinct through worldwide efforts at research into and the subsequent development of vaccines. Ironically, advances in medicine and technology have fostered the emergence of a new group of infectious disorders. Immunosuppressive agents have created a population of compromised hosts and, with this, a new range of infectious diseases. The use of devices such as implants and synthetic valves and vessels has also presented the medical community with the problem of compromised organs, and this has in turn led to a new group of infectious diseases.

Examples of new viruses that have emerged over the past two decades are the human immune deficiency virus and enterovirus type 70.

In this issue, Al Faran et al[1] report on an epidemic of acute hemorrhagic conjunctivitis caused by enterovirus type 70 that occurred in Saudi Arabia. This is a new enterovirus that causes acute hemorrhagic conjunctivitis and was first described from Africa in 1969. The disease was then called "Apollo conjunctivitis," referring to the launch of the Apollo spacecraft to the moon which coincided with the epidemic. The virus's more frequent appearance and the problems it creates for practitioners is a commentary on the nature of these new pathogens in general and the problems they pose for the medical community.

New viral infections continue to emerge, placing constant pressure on the medical community to research for new ways to diagnose, treat, and prevent viral infections. The most impressive difference between medical research today and that of fifty years ago is the prodigious scale on which it is now conducted, along with the incredible diversity of its applications. Scientists and researchers now have at their disposal a multiplicity of facilities that can achieve worthwhile results in short order and with considerable regularity. Today's researcher also has available a boon of information resources to assist in the process of piecing together information on these new threats to health among humans. Improved technology and scientific methods also keep pace with demand. Vaccines are the answer to eradication of viral diseases and there is constant hope for their speedy development, especially for diseases such as HIV. Medical science has constantly accepted and met the challenge posed by these new threats to the health of mankind, and now indisputably represents today's version of the mother of invention.

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Reference

1. Al Faran MF, Tabbara KF, Al-Kassimi HM, et al. Acute hemorrhagic conjunctivitis: an enterovirus type 70 outbreak in Gizan, Saudi Arabia. Ann Saudi Med 1990;10(5):549-52.

Original Articles

CHRONIC RENAL FAILURE IN CHILDREN IN SAUDI ARABIA

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تضم هذه الدراسة مائة طفل (نسبة الذكور للإناث ٦٥ : ٣٥) يعانون من قصور كلوي مزمن، أحيلوا إلى وحدة الكلى لدينا من أماكن مختلفة من المملكة على مدار ثلاثة أعوام، تراوحت أعمار المرضى بين العام الواحد وثلاثة عشر عاما (متوسط العمر أربع سنوات). كان شوه السبيل البولي أكثر أسباب القصور الكلوي المزمن (٣٤ طفلا) تليه الاضطرابات الوراثية العائلية (١٨ طفلا) فنقص التنسج/الثدن الكلوي (١٧ طفلا) ثم اعتلال كبيبات الكلى (١٤ طفلا) فأمراض مختلفة (٥ أطفال). وقد تعذر تشخيص أسباب القصور لدى ١٢ مريضا نظرا لتأخر إحالتهم. ومن بين المرضى الأربعين الذي عولجوا في المرحلة النهائية من قصور الكلى، يخضع ٢٢ مريضا للديال الصياني، ١٣ للديال الصفاقي النقال المتواصل، ٩ للديال الدموي، وأجريت عملية نقل الكلية لتسعة مرضى، توفى سبعة وأخرج مريضان على المعالجة التقليدية المحافظة.

This study includes 100 children (male to female ratio, 65:35) with chronic renal failure referred to our renal unit from different parts of the Kingdom over a period of three years. Their ages ranged from 1 to 13 years with a median age of 4 years. Malformations of the urinary tract were the most common cause of chronic renal failure (N = 34) followed by heredofamilial disorders (N = 18), renal hypoplasia/dysplasia (N = 17), glomerulopathies (N = 14), and miscellaneous diseases (N = 5). No diagnosis could be made in 12 patients because of late referral. Of the 40 patients treated for terminal renal failure, 22 are on maintenance dialysis, 13 on continuous ambulatory peritoneal dialysis, and nine on hemodialysis; nine patients have undergone transplantations, seven died, and two were discharged home on conservative treatment.

The outlook for children with chronic renal failure (CRF) has changed over the last two decades, largely due to the advances made in dialysis and organ transplantation. Children who not very long ago would have faced certain death can now be treated and rehabilitated, so that they can become useful members of the society.

Epidemiological studies of the disease in children are important in order to plan for their special medical requirements, including dialysis and organ transplant facilities. The subject has been researched and discussed extensively in many countries, but very little information is available from the Kingdom of Saudi Arabia. The purpose of this study was to identify the common causes of CRF, assess the problems related to its treatment, and discuss the therapeutic modalities available locally.

Patients and Definitions

The study included 100 children with CRF referred to our renal unit from different parts of the Kingdom over the last three years. Neonates who died soon after birth due to severe renal impairment as in Potter's syndrome were excluded from the study. The definitions used were as follows:[1,2] chronic renal failure (CRF): irreversible increase of serum creatinine levels to more than 180 μmol/L (2 mg/dl); preterminal renal failure: CRF before reaching terminal renal failure; ter-

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minal renal failure: CRF requiring dialysis or transplantation or leading to death.

Results

Fifty-seven (57%) patients were less than 6 years old on admission and this included 22 children younger than a year (Table 1). Seventy-six (76%) children were Saudis and the remaining 24% were children of Arab expatriates working in the Kingdom. A majority of the patients (69%) lived outside Riyadh in different parts of the Kingdom.

Malformation of the urinary tract was the most common underlying renal pathology in 34 cases, followed by heredofamilial disorders in 18, renal hypoplasia/dysplasia in 17, and glomerulopathies in 14. In 12 patients primary pathology could not be identified mainly because of late referral. Further distribution of the individual diseases is shown in Table 2.

Thirty-five (35%) patients were admitted with terminal renal failure. Of these, 15 were less than 5 years old, nine were 5 to 9 years old, and 11 were more than 10 years old. Included were five patients with malformations of the urinary tract, nine patients with heredofamilial disorders, seven patients with renal hypoplasia/dysplasia, three patients with glomerulonephritis, and one each with sickle cell nephropathy, cortical necrosis, and the accidental removal of a single horse-shoe kidney. No cause could be identified in eight patients.

Over the last three years, five more patients progressed to terminal renal failure. The outcome of 40 such patients is shown in Table 3. Twenty-two patients are on maintenance dialysis, 13 on continuous ambulatory peritoneal dialysis (CAPD), and nine on hemodialysis. They have been on this mode of treatment for 4 to 25 months (mean, 14 months). Nine (22.5%) patients received kidney transplants, eight in the Kingdom and one abroad. Of those who underwent transplantation locally, six received cadaver organs and two live related grafts. The one who underwent transplantation abroad received a live, nonrelated transplant. The youngest patient to undergo transplantation in the Kingdom was 5 years old. Seven patients died and that included four infants under 6 months of age. At the time of death, four patients were on conservative treatment, two were on hemodialysis, and one was on CAPD. Two patients, a 6-month-old infant with oxalosis and an 8-year-old girl with severe mental retardation and other handicaps, were discharged home on conservative treatment after discussions with the parents.

TABLE 1. *Age and sex distribution of children with chronic renal failure.*

	Age in years				
Sex	<1	1–5	6–10	>10	Total
Male	13	26	18	9	66
Female	9	9	9	7	34
Total	22	35	27	16	100%

TABLE 2. *Primary renal disease in children with chronic renal failure.*

Etiology	No.of cases*	Total
Malformations of the urinary tract		34 (34%)
Posterior urethral valve	17 (1)	
Reflux nephropathy	10 (2)	
Neurogenic bladder	6 (2)	
Bladder neck and urethral obstruction	1	
Heredofamilial disorders		18 (18%)
Polycystic disease	6 (1)	
Nephronophthisis†	5 (3)	
Oxalosis	5 (5)	
Cystinosis	1	
Alport's syndrome	1	
Renal hypo-/dysplasia without obstruction	17 (7)	17 (17%)
Glomerulopathies		14 (14%)
Infantile nephrotic syndrome	5	
Hemolytic-uremic syndrome	2	
Mesangioproliferative glomerulonephropathy	(1)	
Focal segmental sclerosis	2 (1)	
Crescentic glomerulonephritis	2	
Chronic (idiopathic) glomerulonephropathy	2 (1)	
Miscellaneous		5 (5%)
Sickle cell nephropathy	(1)	
Cortical necrosis	2 (1)	
Neurofibromatosis	1	
Accidental removal of a single kidney	(1)	
Not classified (idiopathic)	12 (8)	12 (12%)
Total	100 (35)	

* The number in parentheses is the number of cases presenting with terminal renal failure.

† Two had Laurence-Moon-Biedl's syndrome.

Discussion

The incidence of CRF among children in Saudi

TABLE 3. *Fate of patients with terminal renal failure in relation to their ages at the time of study.*

		Age (yr)		
Outcome	No. of cases	0-4	5-9	>10
On maintenance dialysis	22 (55%)			
Chronic ambulatory peritoneal dialysis		6	4	3
Hemodialysis		3	2	4
Transplanted	9 (22.5%)	–	1	8
Died	7 (17.5%)	5	1	1
Conservative treatment*	2 (5%)	1	1	–
Total	40 (100%)	15	9	16

* Oxalosis and multiple handicaps.

Arabia is not known. In view of insufficient demographic data and a still evolving referral system, it will take a few more years before such information will become available. In our renal unit we have admitted 100 such patients over three years and the number constitutes 15% of the renal admissions and approximately 2 per 1000 of all admissions in the hospital.

Table 4 summarizes the major causes of CRF in our series and compares them with those reported for other series.[2-4] Congenital abnormalities of the urinary tract constitute a single major group in our patients. This may be due to the genetic factors related to a high incidence of consanguineous marriages or to delayed diagnosis and treatment of the underlying abnormality. In contrast to other studies, the incidence of glomerulopathies in our series is very low. This may be due to the strict diagnostic criteria applied to this group, as all cases included were biopsy proven. It is also possible that some of the patients with unclassified disease actually suffered from glomerulonephritis which could not be diagnosed because of late referral.

Half of our patients (54%) with CRF and slightly less than half (43%) of those admitted with terminal renal failure were under 5 years of age. Treatment of younger patients poses unique problems that are related mainly to their total dependence on others for day-to-day care, including drug and dietary requirements, and the technical difficulties of chronic dialysis, in particular hemodialysis. Repeated and prolonged hospitalization with frequent separation from the family is known to affect the psychosocial development of smaller children. In the Kingdom the problem is occasionally aggravated by attendants (maids) who are hired to care for the children but make a poor substitute for parental care and affection, and inadvertently increase the separation of the patient from the parents.

Included among our dialysis patients were four infants, one baby with severe brain damage secondary to birth asphyxia, one with severe mental retardation with multiple handicaps, and a pair of twins with oxalosis. In view of their ages, other handicaps, and the long-term outlook of their primary pathology, the medical team in our unit favored conservative treatment, but the parents opted for dialysis. One infant died a few months later whereas the remaining three have been on dialysis for the last 6 to 14 months. The ethical and moral issues raised in such situations are not unique to the Kingdom. A very careful approach is needed in helping parents make a rational and informed decision, taking into consideration their social circumstances, cultural perceptions, and religious beliefs.

Regular follow-up of children with CRF is necessary to monitor their renal function, drug and dietary compliance, and growth and development. It is even more important in patients on dialysis because of the additional risk of complications.

TABLE 4. *Major causes of chronic renal failure in children according to different surveys.*

Etiology	This study (Saudi Arabia) (N = 100)	FRG (Pistor et al, 1985[3]) (N = 623)	Sweden (Helin & Winberg, 1980[2]) (N = 77)	France (Broyer, 1984[4]) (N = 391)
Malformations of the urinary tract	34%	29%	29%	16%
Heredofamilial disorders including nephronophthisis and polycystic kidneys	18%	19%	31%	26%
Hypoplastic/dysplastic kidneys	17%	13%	9%	17%
Glomerulopathies (hemolytic-uremic syndrome excluded)	14%	20%	23%	26%
Others	17%	19%	8%	15%

Most of our patients (70%) were referred from places between 100 to more than 1000 km away from Riyadh. In many, including those on CAPD, there were difficulties in organizing the follow-up in the local hospital, mainly due to lack of expertise. This resulted in irregular and infrequent attendance, longer hospital stays than necessary, and sometimes crucial delays in the diagnosis and treatment of life-threatening complications. In a few instances, such problems led to the resettlement of the patient and family in Riyadh.

Nothing is more important than prevention, and with the facilities available in the Kingdom many children can be saved from irreversible renal damage. In nearly half of our patients the primary pathology was such that the patient must have had symptoms like poor urine stream, dribbling, enuresis, or recurrent urine infection which unfortunately were not investigated and treated early. Examination of the fetal urinary system during antenatal ultrasonography can help diagnose many renal abnormalities, particularly the obstructive type.[5] This should give the physician enough time to educate and prepare the parents and to organize referral of the baby to the appropriate center after birth. Similarly, the importance of diagnosing urinary tract infection in children, particularly the younger ones, cannot be over emphasized. In our patients with recurrent urinary tract infections, the appropriate investigations revealed underlying congenital renal abnormalities in about 60% of the cases.[6] Early detection of abnormalities such as vesicoureteric reflux, neurogenic bladder, and posterior urethral valves translates into early appropriate treatment, and this can save many children from serious renal damage.

In conclusion, the rapid advances made by the Kingdom in health care now need to be extended to primary health care, ensuring the detection of most congenital disorders at an early stage. Failure to recognize the symptoms and importance of urinary tract infection remains a matter of major concern. For those children who will inevitably still present with CRF a new chapter has already opened. The availability of treatment makes unexpected demands not just on the medical staff, but also on parents, teachers, social workers, health visitors, and all the other professions involved in the care and upbringing of affected children.

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SHEEHAN'S SYNDROME: A RETROSPECTIVE REVIEW OF 50 CASES SEEN AT RIYADH, SAUDI ARABIA

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روجعت سجلات خمسين مصابا بمتلازمة شيهان، عولجوا جميعا في مستشفى الرياض المركزي. أظهر تحليل البيانـات السريرية والهـرمونية قصة نزف إبان الولادة لدى ٩٤٪ من الحالات. تراوحت الفترة بين بداية ظهور الأعراض والتشخيص بين ٦ أشهر و ٣٣ عاما. كانت هناك أعراض قصور القُندية لدى ١٠٠٪ من الحالات، وقصـور الدرقية لدى ٩٦,٩٪ وقصور الكظرية لدى ٧٠٪. ظهر السلوك الذهاني على نسبة ٢٢٪ من المرضى وسرعان ما خفت حدته بعد المعالجة بتعويض الهرمونات. وبناء على الصيغة الهرمونية لدى المرضى الذين توفرت عنهم بيانات فقد ظهر فقدان موجه الجسد وموجه القُند لدى ١٠٠٪، وفقدان موجه الدرقية في ٨٤,٦٪ وفقدان موجه القشر في ٧٠,٧٪.

The case records of 50 patients with Sheehan's syndrome were reviewed. All patients had been treated at Riyadh Central Hospital. Analysis of the clinical and hormonal data revealed a history of peripartum hemorrhage in 94% of the patients. The interval between the start of symptoms and diagnosis ranged between 6 months and 23 years. There were symptoms of hypogonadism in 100%, hypothyroidism in 96.9%, and hypoadrenalism in 70%. Twenty-two percent of the patients exhibited psychotic behavior, which abated once hormonal replacement therapy was instituted. Hormonal profiles were constructed and revealed somatotrope loss in 100%, gonadotrope loss in 100%, thyrotrope loss in 84.6%, and corticotrope loss in 70.7%, for those patients for whom hormonal data existed.

Pituitary necrosis with partial or panhypopituitarism in the context of peripartum hemorrhage was first recognized by Sheehan in 1937,[1] who estimated that over 50% of patients with shock after postpartum hemorrhage will eventually suffer hypopituitarism.[2] Therefore, all patients who bleed in the peripartum period should be monitored for the possible evolution of hypopituitarism.

Sheehan's syndrome is rarely seen in developed countries and has an incidence of one per 10,000 deliveries.[3] This low incidence is attributed to the existence of good perinatal and obstetrical care. The disorder is more frequently seen in areas where home deliveries are common as well as in areas where health care is not yet well developed.

The Kingdom of Saudi Arabia has witnessed a dramatic improvement in its health care system over the past fifteen years but the spectrum of Sheehan's syndrome in the Kingdom has not been assessed. Therefore we conducted a retrospective analysis of patients with Sheehan's syndrome that was diagnosed over a period of 8 years (1980–1988) at Riyadh Central Hospital. This hospital is a 1130-bed referral center, with patients coming from all over the Kingdom.

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Material and Methods

The case records of all patients with Sheehan's syndrome seen between 1980 and 1988 at Riyadh Central Hospital were reviewed. Clinical evidence of Sheehan's syndrome was regarded as the presence of symptoms or signs of partial or complete pituitary insufficiency against a background of previous obstetrical injury. Information concerning the parity of the patients, site of delivery, nature of obstetrical insult, and history of blood transfusion was also sought. Also noted were descriptions of physical signs of endocrine gland failure that related to the ovaries, thyroid, and adrenals, and as indicated by the absence of axillary or pubic hair, atrophy of the breast, dryness of the skin, bradycardia, and hypotension.

Laboratory data sought included: complete blood count (CBC), electrolyte determinations, and hormonal investigations, namely: thyroid function tests (T4 RIA, T3 RIA, TSH), plasma luteinizing hormone (LH), follicle-stimulating hormone (FSH), and random cortisol as well as cortisol and growth hormone levels measured after insulin-induced hypoglycemia.[4]

All measurements were done using standard radioimmunoassay methods, but because of the irregular availability of assay reagents during the first three years under review, not all patients had full biochemical confirmation of the disease.

Two sets of inclusion criteria were applied in this study: The first consisted of the presence of clinical features. These included evidence of failure of two or more of the pituitary-dependent endocrine glands in the context of a severe postpartum or antepartum hemorrhage and in the absence of any other causes for the endocrine insufficiency, as well as the absence of symptoms suggestive of pituitary tumor such as headache, blurred vision, or visual field limitation with hormonal data suggestive of hypothyroidism (low serum thyroxine level) and/or hypoadrenalism (low serum cortisol level) also ruling out patients from the study. The second set of criteria consisted of the above clinical criteria plus biochemical confirmation, that is, hormonal assay proving secondary failure of at least one pituitary-dependent endocrine gland.

Patients who fulfilled the first criteria constituted highly probable cases of Sheehan's syndrome, and those who also had hormonal confirmation constituted definite cases. The data for both groups were analyzed together. In determining the frequency of occurrence of individual pituitary cell failure, only data from those patients who had had a hormone profile done were analyzed.

Results

Fifty-six patients were initially diagnosed as having Sheehan's syndrome for the 8-year period studied. Six were eliminated because they did not fulfill the inclusion criteria. Of the remaining 50 patients who fulfilled one or both sets of criteria, 40 were considered definite cases and 10 as highly probable. Forty-six were Saudi, two were Yemenis, one was Egyptian, and one was Palestinian. Age at onset of symptoms ranged between 19 to 51 years (mean, 32.2 ± 7.3 years; median, 31 years). The ages at the time of diagnosis ranged from 26 to 60 years (mean, 40.4 ± 7.8 years; median, 40 years). The interval between the start of symptoms and ultimate diagnosis ranged between 6 months and 23 years (mean, 8.6 ± 6.4 years). Figure 1 illustrates the age distribution of patients at the onset of symptoms and at diagnosis.

It was difficult to objectively assess the history of bleeding in most patients because they delivered their babies at home. The parity of the patients ranged from one to 12 with a mean of six in 24 patients. Forty-three patients had a history of postpartum hemorrhage and four had had antipartum hemorrhage. The remaining three patients had no history of excessive bleeding.

Thirteen patients gave a history of blood transfusions and eight denied any history of transfusion. This information was lacking in the others. For the 40 patients in whom this information was available, 33 delivered at home and seven in hospitals.

Table 1 shows the breakdown of symptoms and signs of pituitary failure among the patients in the study. Psychotic behavior was present in 11 patients, and it was the presenting feature in nine. Other prominent manifestations included menstrual irregularities, failure of lactation, weakness and loss of weight, and absent or sparse axillary and pubic hair.

Routine laboratory investigation at the time of presentation revealed significant hyponatremia (< 129 mmol/L) in 18 (36%) and mild hyponatremia (Na+ 130–134 mmol/L) in four (8%).

TABLE 1. *Clinical manifestations in patients with Sheehan's syndrome.*

Clinical features*	No. affected	Percentage
Menstrual irregularities (N = 48)		100
Amenorrhea	46	
Oligomenorrhea	2	
Absent or sparse axillary and pubic hair (N = 40)	40	100
Weakness and loss of weight (N = 42)	42	100
Dryness of skin (N = 33)	32	96.9
Failure of lactation (N = 45)	43	95.5
Atrophy of the breast (N = 20)	18	90
Hypotension (≤ 90/60) (N = 50)	20	40

* Numbers represent those patients for whom data were available.

Anemia without any other obvious cause (hemoglobin, < 120 gm/L) was present in 33 (66%) patients (mean, 102.4 ± 1.4 gm/L).

Tables 2 and 3 summarize the results of the hormonal data for the 45 patients in whom endocrine function tests were done.[4]

Discussion

Pituitary necrosis in patients with postpartum hemorrhage is believed to be caused by occlusive spasm of the arteries that supply the anterior pituitary, thus leading to ischemia and necrosis.[5]

The clinical features of hypopituitarism vary from partial to panhypopituitarism.[6,7] This is illustrated in Table 1, where it is shown that 100% of our patients were amenorrheic or oligomenorrheic and 95.5% failed to lactate. Lethargy, bradycardia, and dryness of skin with possible

TABLE 2. *Thyroid hormone and gonadotrope levels in patients with Sheehan's syndrome.*

Hormone	Reference interval	Total number studied	Number with abnormal results	Range*	Mean ± SD
T3 RIA (nmol/L)	1.2 - 3.4	45	36	0.1 - 0.94	0.5 - 0.2
T4 RIA (nmol/L)	51 - 42	45	33	5.1 - 48.9	18.4 - 13
TSH (mU/L)	1 - 10	39	30†	0.5 - 9.6	4.3 - 12.3
LH (IU/L)		29	20††		
< 45 y.o.	2 - 20	18	18	1.2 - 13	4.5 - 3.5
> 45 y.o.		11	11	1.3 - 18	6.2 - 4.8
FSH (IU/L)		29	29††		
< 45 y.o.	2 - 50	18	18	1.0 - 12.7	5.8 - 3.9
> 45 y.o.		11	11	3.3 - 10.4	7 - 3.4

* Values for those with abnormal results.

† The range values of TSH were considered inappropriate for the low T4 and T3 values.

†† The range values of LH and FSH were considered inappropriately low for amenorrheic patients, especially for postmenopausal age.

T3 = triiodothyronine; T4 = thyroxine; RIA = radioimmunoassay; TSH = thyroid stimulating hormone; LH = luteinizing hormone; FSH = follicle stimulating hormone.

TABLE 3. *Cortisol and growth hormone levels in patients with Sheehan's syndrome with insulin tolerance test.*

	Cortisol			Growth hormone		
Time	N*	Range	Mean ± SD	N*	Range	Mean ± SD
Baseline	29	5.5 - 107.6	41.1 ± 31	29	0.2 - 3.1	1.1 ± 0.7
	12	113 - 400	254.0 ± 105			
30 min.	21	5.5 - 82.7	37.3 ± 23.2	19	0.25 - 2.5	1.3 ± 0.6
	4	193 - 402.8	295.1 ± 95.8			
60 min.	21	8.2 - 100	45.7 ± 29.8	13	0.25 - 4.1	1.2 ± 1
	4	220 - 403	304 ± 92.4			

* Number of patients with hormonal data.

† Range of hormonal data for cortisol data was divided into two groups: (1) with cortisol below normal range and (2) the other with cortisol in the normal range; normal range for cortisol (110 - 520 nmol/L) and for growth hormone (0.0 - 10 μg/L).

hypothyroidism were seen in 96.9%. Weakness, weight loss, and hypotension with possible hypoadrenalisms were observed in 70% of our patients.

Significant hyponatremia was seen in 18 patients and four had mild hyponatremia; nine of the patients were hypotensive. All patients were normokalemic. Hyponatremia in patients with Sheehan's syndrome[2] is due to deficient quantities of total sodium in the body, water retention, and transfer of electrolytes between tissues and plasma, all of which together may lead to hyponatremia.

The psychotic behavior seen in 11 patients was the presenting feature in nine. A wide spectrum of psychiatric disorders was seen. Six patients exhibited disorientation, hallucinations, and restlessness. The other five had depression, confusion, and insomnia. Three of the patients with an acute psychosis were first admitted to psychiatric hospitals before Sheehan's syndrome was diagnosed. All 11 patients responded favorably to steroid therapy.[8]

Hormonal data on patients who had undergone evaluation revealed gonadotrope loss in 96.5%, which was second only to somatotrope loss, with a frequency of 100%. Thyrotrope loss occurred in 84.6% and corticotrope loss in 70.7% of the patients.

Loss of growth hormone reserve was noted for all patients who underwent the insulin tolerance test. This represents an early sign of pituitary failure.[5]

Of the 12 patients who showed no clinical or biochemical indications of adrenal insufficiency, Sheehan's syndrome was diagnosed in nine within five years of the obstetrical insult. This agrees with the observations of others.

The varying degrees of damaged pituitary cells observed in our patients is in keeping with the observations of others, in that there can be partial or complete damage to the pituitary.[6] The data on the pituicyte findings in our patients are summarized in Table 4.

Patients were treated with steroid and thyroxine, based on their clinical and hormonal data. Estrogen and progesterone were given to patients less than 45 years old, but induction of ovulation was not attempted in any patients.

TABLE 4 *Frequency of failure of pituicytes in Sheehan's syndrome.*

Pituitary cell type	Number of patients with failure*	Percentage
Somatotrope	29/29	100
Gonadotropes	29/29	100
Thyrotropes	33/39	84.6
Corticotropes	29/41	70.7

* Patients for whom hormonal data were available.

Most of the patients were seen regularly and were doing well on replacement therapy. Steroid requirements in such patients are less than those in patients with primary adrenocortical failure. Most patients in our study were on prednisone (2.5 to 5 mg or equivalent per day), which may suggest partial rather than complete destruction of the corticotropes.[9]

We believe that, with the improved health care in this country, less patients will suffer from postpartum hemorrhage and, along with this, fewer patients with Sheehan's syndrome will be seen.

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SINUSITIS IN SAUDI CHILDREN

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يعتبر التهاب الجيوب الأنفية واحدا من أكثر الأمراض شيوعا لدى الأطفال، على الرغم من عدم تحديد أرقام فعلية في الأدب الطبي. أظهرت هذه الدراسة، التي أجريت على مراجعي العيادة الخارجية في مستشفى الملك فيصل التخصصي ومركز الأبحاث، وهو مستشفى إحالة في المملكة العربية السعودية، أن نسبة انتشار التهاب الجيوب الأنفية بين المراجعين في عام ١٩٨٨م هي ٨,٥٪. كان السعال أكثر الأعراض تواردا (٥٤٪)، بينما كان الثرّ الأنفي المتواصل أول الأعراض ظهورا في نسبة ١٥٪ فقط. أما أكثر العوامل المؤهبة تواترًا فقد كانت الحساسية (٢٦٪)، يليها ضخامة الغدانيات (٢٥٪) ثم انحراف الوتيرة (١٣٪). وتناقش هذه الدراسة بعض العوامل الهامة الأخرى كانخفاض نسبة الرطوبة في الرياض مثلا.

Sinusitis is considered one of the most common diseases in childhood, though no actual figures are quoted in the medical literature. This study, which was conducted in an ambulatory care facility at King Faisal Specialist Hospital and Research Centre in Riyadh, a referral center for all of Saudi Arabia, revealed a prevalence rate for sinusitis of 8.5% among new patients seen during 1988. The most common presenting symptom was cough (54%), while persistent rhinorrhea accounted for only 15% of the presenting symptoms. The most frequent predisposing factor was allergy (26%), followed by hypertrophied adenoids (25%) and septal deviation (13%). Other important factors, such as the low relative humidity in Riyadh, are also discussed.

Sinusitis is a common problem in children and is one of the most common diseases of children.[1-3] It is more prevalent than generally recognized and may even be found in newborns.[4] It is often missed, however, because pediatricians frequently do not recognize or treat sinus disease properly.[1] Also, many radiologists cannot interpret sinus x-ray studies in young children, on the assumption that sinuses are not developed prior to the age of two years, though maxillary sinus cavities are usually roentgenographically visible by 2 to 3 months of age.[5] Children with chronic rhinorrhea are frequently dismissed as being "just allergic."[6] Sinusitis is considered common in Saudi Arabia,[7] but it is difficult to find any mention of a specific incidence in any literature on the topic.[8] Most authors just state that sinusitis is common in children.[1,7,9,10] This study was undertaken to reveal the prevalence of sinusitis among Saudi children, particularly in the Riyadh area.

Patients and Methods

Included in the study were all patients with a positive radiological diagnosis of sinusitis seen by me in an ambulatory care facility, at the King Faisal Specialist Hospital and Research Centre, from January through December 1988. X-ray studies were considered positive if there was opacification of one or more sinuses, an air-fluid level in the maxillary sinuses, or mucosal thickening of greater than 4 mm.

Patients with chronic or recurrent symptoms underwent more studies, including assessments for immunoglobulins, IgG subclasses, IgE, sweat chloride, and nasal smear for eosinophils and polymorphonuclear cells. The nasal smear was repeated following therapy if the first was negative for eosinophils. Patients with middle-ear effu-

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sion had tympanometric studies. Most patients were from Riyadh and the rest came from various regions within the Kingdom. Depending on the duration of symptoms, all patients received a two- to three-week course of amoxicillin, except for two patients who were allergic to penicillin and were given trimethoprim-sulfamethoxazole. A follow-up x-ray study was taken 3 to 4 weeks after the beginning of therapy and was clear in all but four patients. These four patients received a second course of treatment with a different antibiotic, either amoxicillin clavulanate potassium or trimethoprim-sulfamethoxazole, which was followed by improvement or complete clearance.

Results

A total number of 74 cases occurred in 69 patients, with five recurrences seen during the study year. These represented 8.5% of all new patients seen by me during the same period. Patient age ranged from 7 months to 14 years (mean, 5 years). There were 43 males (62%) and 26 females (38%) (Figure 1).

Duration of symptoms was as follows: less than 1 month (i.e., acute) in 64% of patients (36% had symptoms for less than 1 week and 28% had symptoms for 1-4 weeks); 1-3 months (i.e., subacute) in 7% of patients; and more than 3 months (i.e., chronic) in 29% of patients.

The most common presenting symptom was cough, and was the main symptom in 54% of patients; 12 patients (16%) had a chronic or recurrent cough and 28 patients (38%) had a recent cough or presistent upper respiratory infection. Wheezing or exacerbation of unremitting asthma was the presenting symptom in 15 patients (20%). All of these latter patients were seen several times in the emergency room or other clinics yet a diagnosis of sinusitis was never contemplated.

The third most common presenting symptom was fever, which occurred in 12 patients (16%), followed by rhinorrhea in 11 patients (15%). Many patients had several presenting symptoms but none presented with fetor oris, though it was encountered in many patients. None presented with, or developed, any serious complication. The frequency of presenting symptoms is summarized in Table 1.

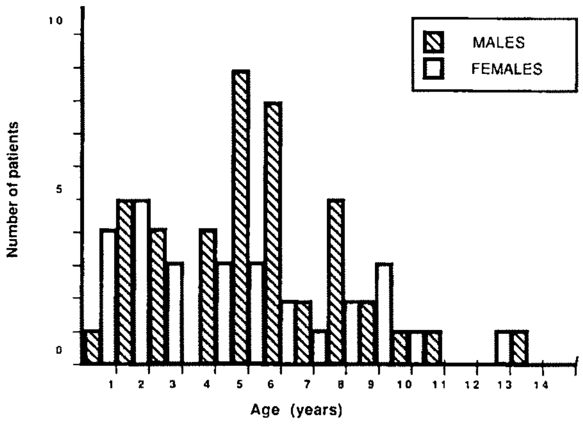

FIGURE 1. Age and sex distribution of 69 children with sinusitis.

TABLE 1. *Frequency of presenting symptoms in 69 patients with 74 episodes of sinusitis.*

Symptom	No. of episodes (N = 74)
Cough	40 (54%)
Chronic or recurrent 12 (64%)	
Recent or persistent 28 (38%)	
Wheezing or exacerbation of asthma	15 (20%)
Fever	12 (16%)
Rhinorrhea	11 (15%)
Obstructed nostrils	6 (8%)
Headache	6 (8%)
Epistaxis	3 (4%)
Vomiting	3 (4%)
Dizziness	2 (3%)
Recurrent sore throat	2 (3%)
Hearing loss	1 (1%)

Predisposing factors were found in 55 patients (80%) with allergy, based on signs and symptoms and positive nasal smear for eosinophils or increased serum IgE, accounting for 26% of cases, followed by hypertrophied adenoids in 25% of cases and septal deviation in 13% of cases. Immunological causes were found in six patients (9%); four had IgG_2 subclass deficiency, one had a low IgA level, and one patient was nephrotic. None of the patients had cystic fibrosis. Predisposing factors are summarized in Table 2.

The most frequent associated finding was middle ear effusion, which occurred in 21 cases (28%), followed by wheezing in six patients (8%). Five patients had had a documented sinusitis in the previous years and five had a recurrence during the year of study. Five patients had at one time had a tympa-

TABLE 2. *Predisposing factors found in 55 of the 69 children.*

Factor	No. of children
Allergy	18 (26%)
Hypertrophied adenoids	17 (25%)
Septal deviation	9 (13%)
Immunodeficiency	6 (9%)
Hypertrophied turbinates	5 (7%)

TABLE 3. *X-ray findings tabulated according to type of involvement and frequency of sinuses involved in 74 cases.*

	Unilateral	Bilateral
Maxillary		
Opacification	16 (22%)	35 (47%)
Mucosal thickening	9 (12%)	7 (9%)
Air-fluid level	1 (1%)	1 (1%)
Ethmoid		
Opacification	10 (13%)	31 (42%)
Mucosal thickening	2 (3%)	7 (9%)
Frontal	1 (1%)	0
Sphenoid	0	0

nostomy and/or adenoidectomy. One patient had bilateral purulent eye discharge that grew beta-lactamase–positive *Hemophilus influenzae.*

Only one patient, a 14-year-old boy, had frontal sinusitis; none had sphenoidal sinusitis. The rest had either maxillary or ethmoidal sinusitis, or both. X-ray findings are summarized in Table 3.

Discussion

This study was conducted in an ambulatory care facility, namely the Polyclinics, at King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia, which is a referral center for tertiary care for patients from all over the Kingdom of Saudi Arabia. Therefore, our patients represent a selected group of mainly chronic or undiagnosed cases. Yet 8.5% of these patients had sinusitis, a figure that is assumed to be less than what may be encountered in a walk-in pediatric clinic or in a private pediatrician's office where more acute illnesses, particularly upper respiratory infections, are seen.

It has been estimated that children have six to eight upper respiratory tract infections per year and that 0.5 to 5.0% of upper respiratory tract infections are complicated by sinusitis.[10,11] One of the most important predisposing factors to sinusitis is allergy,[1,4,9,12] and was found in 26% of our patients. Al-Frayh et al[13] have found the prevalence of allergy among Saudi children ranges from 12 to 25%. The latter figure was found among children in the Riyadh area where most of our patients came from. Al-Nahdi et al[14] found sinusitis in 18% of their allergic patients in the Eastern Province of Saudi Arabia.

While the other predisposing and associated factors in our study group were essentially similar to those reported by others,[1,8-10,12] another important factor that might have played a role in our patients is the dry climate with low relative humidity in the Riyadh area with resulting dryness of the mucosa that affects ciliary action.[1,11] The mean relative humidity in Riyadh during 1988, when the study was conducted, was 25% with a range of 5 to 72%.[15] Furthermore, it is often dusty in Riyadh with many sandstorms.

Four patients did not respond to amoxicillin and required either amoxicillin clavulanate potassium or trimethoprim-sulfamethoxazole. We have to assume, on clinical grounds, that these patients, amounting to 5% of the total, had beta-lactamase-producing bacteria. Chowdhury et al[16] found that 4% of the isolated strains of *H. influenzae* in Riyadh were beta-lactamase producers, while Namnyak et al,[17] in Dammam, found four strains of *Branhamella catarrhalis,* out of nineteen, in patients with bronchopulmonary disease to be beta-lactamase producers. This is less than what was encountered in the United States where an earlier study revealed an average of approximately 11% (15% of *H. infuenzae,* 40% of *B. catarrhalis).*[18] Recent studies from Pittsburgh, however, revealed much higher figures; about three-fourths of cases of *B. catarrhalis* and 30% of *H. influenzae* produced beta-lactamase.[19]

The association of sinusitis and unremitting asthma is well known.[20] Fifteen patients (20%) presented as such and yet all were previously missed when seen in the emergency room or other clinics.

Although we do not have a figure for negative x-ray studies, it is our impression that most of our patients who were suspected, on the basis of history and physical examination findings, to have sinusitis had a positive x-ray study. Wald et al,[18] on the basis of history alone, could predict the occurrence of abnormal radiographs in 80% of their patients (88% of patients younger than 6 years and 70% of patients older than 6 years of age). Some radiologists may underread sinus x-ray examinations and some are reluctant to interpret studies in patients younger than 2 to 3 years of age. In some of our patients maxillary sinuses were described, by one radiologist, as "not developed" on initial x-ray studies while follow-up films, after treatment, interpreted by another radiologist, showed "improvement" or "good clearing" in comparison to initial films. This experience has been reported by others[8] who found that radiologists were reluctant to x-ray sinuses in young children because of difficulty with interpretation. This is most likely a universal problem and pediatricians should train themselves in interpreting their patients' sinus x-ray studies. However, in agreement with the view of Wald et al,[18] it is probably unnecessary to obtain sinus radiographs in the majority of apparently uncomplicated cases of suspected sinusitis in children less than 6 years of age.

The frequency of symptoms was similar to that found by Wald et al,[21] except for the relatively high prevalence of wheezing and exacerbation of asthma in our patients (20%), which is not listed by Wald's group.

We had no patient with cystic fibrosis, which is considered rare in Saudi Arabia, though a recent study by Nazer et al[22] reported 13 cases of cystic fibrosis from Saudi Arabia, suggesting that it may not be as infrequent as suspected.

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ANEMIA OF ACUTE FOCAL INFECTION IN CHILDREN IN THE AREA OF RIYADH

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يترافق الخمج الجرثومي الشامل الحاد منه أو المزمن مع فقر الدم . وتشير هذه الدراسة إلى أن فقر الدم يمكن أن يصاحب الأخماج البؤرية الحادة أيضًا والتي تعالج غالبا في العيادات الخارجية . راجعت مجموعة تضم ٦٨٢ طفلا (تراوحت أعمارهم بين ٦ أشهر و ١٢ عامًا) العيادات الخارجية لمستشفى الأطفال بالسليمانية في الرياض خلال فترة ثلاثة أشهر، بسبب شكاوي مختلفة تضمنت التهاب البلعوم واللوزة، التهاب الأذن الوسطى والتهاب الجيوب الأنفية . اكتشف فقر الدم (الهيموغلوبين أقل من ١٠,٣ غرام) لدى نسبة ٣٦,٥٪ من الأطفال الذين تراوحت أعمارهم بين ٦ و ١١ شهرا، ولدى ٢٢,٧٪ بين ١٢ و ٣٥ شهرا، ولدى ١١,٢٪ بين ٣ أعوام إلى ١٢ عاما . وقد تبين أن للعمر (P< ٠,٠١) ومدة الحمى (P< ٠,٠٢) ترابطا ذا أهمية مع فقر الدم .

Chronic or acute systemic bacterial infection is usually associated with anemia. This study shows that anemia can also be associated with acute focal infections which are usually treated in outpatient clinics. A group of 682 children (aged 6 months to 12 years) were seen in a three-month period in the outpatient clinics of Suliemania Children's Hospital, Riyadh, with varying complaints consisting of pharyngotonsillitis, otitis media, and sinusitis. Anemia (hemoglobin < 10.3 g) was detected in 36.5% of the children aged 6 to 11 months, in 22.7% aged 12 to 35 months, and in 11.2% aged 3 to 12 years. Age ($P < 0.01$) and duration of fever ($P < 0.02$) were found to have significant association with anemia.

Anemia is a frequent finding in children with chronic infection and disorders such as malignancy and rheumatoid arthritis.[1,2] Acute systemic bacterial infection, which usually requires hospitalization, has also been shown to be accompanied by significant anemia.[3-5] Viral illnesses cause anemia by inducing sudden hemolysis in the presence of glucose-6-phosphate dehydrogenase deficiency,[6] immunohemolysis,[7] aplastic anemia,[8] or transient erythroblastopenia of childhood.[9]

The objective of this study was to ascertain whether anemia occurs in children who suffer from the acute localized infections commonly seen and managed in outpatient clinics. These include pharyngotonsillitis, otitis media, and sinusitis.

Material and Methods

Children from all social classes are seen in the emergency room and outpatient clinics of Suliemania Children's Hospital in Riyadh. The clinics are run by pediatric residents and specialists who are supervised by consultants and teaching staff from King Saud University College of Medicine. The routine outpatient laboratory investigations for febrile children include complete blood count (CBC), relevant cultures, and a chest and, when indicated, a sinus x-ray study. Children (aged 6 months to 12 years) who were seen in the outpatient clinics during September, October, and November of 1987 for pharyngotonsillitis, otitis media, or sinusitis were enrolled in this prospective study. Appropriate history was taken and physical examination was done. Also recorded were oral or rectal temperature, dura-

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tion of fever, and the clinical diagnosis, taking into consideration the clinical observations and recommendations made by others.[10,11] CBC was determined on a Coulter Model S plus II Counter. Using the approach of Ghafouri et al,[12] anemia was defined as: hemoglobin (Hb) concentration less than 103 gm/L for children aged 6 to 59 months; Hb less than 112 gm/L for children aged 5 to 8 years; and Hb less than 119 gm/L for male and less than 124 gm/L for female children older than 8 years. The effects of age, duration of fever, and site of infection on the presence of anemia were studied.

Statistical analysis was done using the unpaired *t* and chi-square tests. Exclusion criteria included all febrile patients suspected of having chronic or acute systemic infection which required hospital admission. In addition, similar to other studies, febrile infants of less than 6 months of age were excluded from the study because they may have serious systemic bacterial infection without alarming clinical or laboratory indicators.[13]

Results

A group of 682 febrile children (aged 6 to 144 months; mean age, 20.76 ± 18.96 SD) were seen in the outpatient clinics (Table 1). There were 626 cases of tonsillitis/pharyngitis (including 10 cases with simultaneous otitis media which was regarded as pharyngotonsillitis in the statistical analysis), 43 cases of otitis media, and 13 cases of sinusitis (Table 2).

Anemia (mean Hb, 9.75 ± 0.67 gm SD) was detected in 137 (20%) patients. In these 137 patients, the prevalence of anemia was as follows: 128/626 (20.4%) cases with pharyngotonsillitis, 6/43 (14%) with acute otitis media, and 3/13 (23%) with sinusitis. It is difficult to do a statistical comparison in the sinusitis group due to its small size. However, comparison of pharyngotonsillitis cases and otitis media cases was possible and showed no statistically significant difference ($P > 0.40$).

When narrower age ranges were considered, it was found that infants between 6 and 11 months had a much higher prevalence of anemia (36.5%) than did the remaining groups. Prevalence in children at 12 to 35 months was 22.7%; at 36 to 59 months, 13%; and at 60 to 144 months, 10%, with a P value < 0.01.

TABLE 1. *Age distribution among 682 children with acute focal and 137 with acute infection and anemia seen in outpatient clinics.*

Age (mo)	Children with AFI (N = 682)	Anemic children (N = 137)	Percentage of anemic children
6 - 11	123	45	36.5
12 - 35	255	58	22.7
36 - 59	124	16	13
60 - 144	180	18	10

AFI = acute focal infection.

TABLE 2. *Age and site of infection distribution among 137 children with and 545 without anemia seen in outpatient clinics.*

	Pharyngo-tonsillitis		Otitis media		Sinusitis	
Age (mo)	A	NA	A	NA	A	NA
6 - 11	43	69	2	9	0	0
12 - 35	54	180	3	14	1	3
36 - 59	15	97	1	8	0	3
60 - 144	16	152	0	6	2	4
Total	128*	498	6*	37	3	10

A = anemia; NA = not anemic.
* $P > 0.40$

Forty-two of the anemic children were seen for re-evaluation after 3 to 4 weeks, and at that time, 39 had a normal Hb level.

Thirty-five (25.5%) children had fever that lasted for more than four days (mean, 5.43 ± 0.60 days SD), and fever lasted less than four days in the remaining 102 (mean, 2.2 ± 1.2 days SD). The 35 children with longer duration of fever had a lower Hb level (mean, 898 ± 82 gm SD) than did the remaining 102 children (mean, 995 ± 46 gm SD); the difference was statistically significant at $P < 0.02$. Comparison of the average age of these two groups of children using Student's *t* test showed no statistically significant difference ($P > 0.7$).

Discussion

Chronic[1,2] or acute[14] systemic infection seems to be one of the most common causes of reduced Hg concentration during childhood. Anemia, which usually correlates with the severity of infection,[3] has been documented in children with acute systemic infections[3,4] that require hospitalization. In the present study, anemia was seen in children with acute pharyngotonsillitis, otitis media, and sinusitis. Although 93% of these children had pharyngotonsillitis, the site of infection did not display a significant association with the development of anemia. Anemia was frequent in children younger than 36 months (27.2%) and was predominant in those who were 6 to 11 months old (36.5%). The lower Hb level (< 95 gm/L) in the anemic group was recorded among children whose febrile illness had lasted four days or more before they were seen in the outpatient clinic.

In the anemia that occurs with chronic diseases, there is a diminished rate of erythropoiesis as a result of hypoferremia,[4] restricted iron supply,[1] and low levels of erythropoietin,[15] combined with an increased rate of red blood cell destruction.[4] It is likely that certain pathophysiological mechanisms of the anemia associated with chronic infection also operate during acute infection.[14] In the present study, the duration of illness in 74.5% of the children was less than four days, and this short duration cannot account for the rapid drop in the Hb level if a depressed rate of erythropoiesis were the sole mechanism. Therefore, similar to chronic infection, the increased rate of erythrocyte destruction may also be an important factor in the development of anemia of acute infection.

It has been shown that anemia in children such as those in our study is very likely to correct itself spontaneously,[16] and the hematological response to iron therapy in infants with acute minor infections may not necessarily be indicative of iron deficiency.[17] The detailed diagnostic evaluation of mild anemia in children with acute infection becomes necessary only for those whose anemia does not resolve following control of the infection[14] or those who remain anemic more than four weeks after recovery.

The results of this study suggest that infections do not need to be severe or chronic in order for anemia to develop.

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A COMPARISON OF MAXIMAL GASTRIC SECRETION IN CONTROLS AND DUODENAL ULCER PATIENTS FROM THE SUDAN AND THE UNITED KINGDOM

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تم قياس النتاج الأقصى لإفراز الحمض المعدي لدى مجموعات ضبط ومرضى مصابين بقرحة عفجية من السودان والمملكة المتحدة. وتبين أن نسبة الإفراز لدى الذكور من المملكة المتحدة أكثر منها لدى الإناث في كل مجموعة، كما كانت نسبة الإفراز بين المرضى المصابين بقرحة عفجية أعلى، بدرجة هامة. منها بين مجموعات الضبط. بالنسبة للمجموعة السودانية لم يُظهر سوى الذكور المصابين بقرحة عفجية أي دليل على فرط الافراز. أما مجموعة المملكة المتحدة فقد كانت نسبة الافراز المعدي لديهم أعلى بصورة عامة منها لدى نظرائهم السودانيين. كان السودانيون أصغر سنا وأخف وزنا بدرجة ملحوظة من أفراد مجموعة المملكة المتحدة. بعد ضبط هذه العوامل اختفى الفارق بين الاناث المصابات بقرحة عفجية في البلدين، في حين أن نسبة الإفراز لدى الذكور من المملكة المتحدة، وباستثناء الاناث في المجموعتين، كانت أعلى منها لدى نظرائهم السودانيين. كان هناك ترابط إيجابي بين النتاج الأقصى للحمض المعدي ونسبة المدخنين في كل مجموعة. قد يكون التدخين عاملا في حدوث الإصابة بالقرحة العفجية في الذكور من كلا البلدين، ولكن هناك عوامل مؤهبة أخرى بالنسبة للنساء السودانيات.

Maximal gastric secretion was measured in controls and patients with duodenal ulcer from the Sudan and the U.K. Males from the U.K. were found to secrete significantly more than females in each group, and the group with duodenal ulcers secreted significantly more than controls. In subjects from the Sudan, only male subjects with duodenal ulcers showed any evidence of hypersecretion. The U.K. subjects generally exhibited greater gastric secretion than their Sudanese counterparts. The Sudanese were significantly younger and weighed significantly less than the U.K. subjects. After standardization for these factors, the female subjects with duodenal ulcer no longer differed between the countries, and the U.K. males, but not the females, of each group still showed greater secretion than their Sudanese counterparts. Maximal gastric secretion in the males was positively related to the proportion of cigarette smokers in each group. Smoking may be a factor in the occurrence of duodenal ulcer in males of both countries, but some other factor operates in Sudanese women.

An increased maximal gastric secretion in patients with duodenal ulcer has been found in the inhabitants of many parts of the world, including India,[1-3] Hong Kong and Scotland,[4] Nigeria,[5] as well as England.[6,7]

In Hong Kong, for example, Chinese patients with duodenal ulcer secrete about 60% more than controls in response to pentagastrin.[4] Men, whether controls or patients, did not secrete significantly more than women, whereas in the concurrent Scottish series, men did secrete significantly more than women, but this was seen more in patients than controls. This latter finding is typical of Western studies.

In an attempt to ascertain whether such differ-

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ences exist between male and female patients and controls in an African population, maximal gastric secretion was determined in subjects of the U.K. and the Sudan, using similar techniques. The results were standardized for differences in age and weight, and analyzed according to nationality, presence or absence of duodenal ulcer, and sex and smoking status.

Methods

Subjects

Sudanese controls were chosen if there was no history of dyspepsia. U.K. controls were staff or in-patients of the Middlesex Hospital. Most of the U.K. in-patient controls were suffering from non-gastrointestinal conditions, but the 39 who did have gastrointestinal tract symptoms were proven not to have a peptic ulcer by appropriate investigation.

Duodenal ulcer in Sudanese patients was diagnosed if the patients had a typical history and symptoms, and this was confirmed by radiography. Duodenal ulcer in U.K. patients was proven endoscopically or at operation for the ulcer.

Measurements

The sex, age, weight, height, duration of ulcer, and the number of cigarettes smoked per day were recorded for each subject. For social reasons, very few Sudanese females smoke and they were not questioned as to their smoking habit. They were therefore classified as nonsmokers. This classification is not ideal, but since female Sudanese would not admit to smoking even if they did, it is probably the best approximation to the truth. U.K. subjects designated as nonsmokers were lifelong nonsmokers. Exsmokers were classified as smokers because there appears to be a long-term effect of smoking on maximal gastric secretion.[8-10]

Gastric Aspiration and Analysis

After an overnight fast, each subject had a gastric secretion test in the morning. Aspiration was accomplished by nasogastric tube, with the tip of the tube positioned in the stomach by the water-recovery test.[11] After a 10- to 15-minute settling period, a 1-hour basal collection was begun. Samples were taken every 10 to 15 minutes, and the interval was kept constant for any particular test. Just before the end of the basal period, a 25- or 50-mg bolus of Phenergan (promethazine hydrochloride, an H-1 antihistamine) was given intravenously and an intravenous infusion of histamine was begun at a dose of 130 nmol kg^{-1} h^{-1}.[12] Stimulation was continued for about 2 hours with a plateau of secretion reached within 20 to 60 minutes. After the stimulation period had finished, the nasogastric tube was withdrawn and the subject given refreshment.

The volume of each gastric aspirate sample was measured to the nearest milliliter, and the pH was measured by automatic titration to a pH of 7.0, using 100 mmol/L NaOH. Acid output was expressed in mmol h^{-1}. For each maximal histamine period, a plateau of secretion was chosen by an objective method, using a computer program, and the mean maximal acid output calculated.[13]

Statistical Methods

The degree of association between variables was measured by Pearson's correlation coefficient. Linear and multiple regressions were derived by least-squares analysis, with the statistical significance of the slope being calculated by testing against zero with Student's *t* test. Average values are expressed as means, and the *t* test was used to test the difference between means.

The mean ages and weights of the respective groups of the two series were sometimes markedly different. Therefore standardization to a common age or weight was accomplished with the derived regression equations, using a previously published method.[14]

Results

There was a large difference in the ages between the nationalities, and some difference in the weights, especially in the men (Table 1). The Sudanese men were lighter and, as a whole, the Sudanese were younger. In the first instance, therefore, the secretion data were standardized for age and weight by the use of linear regressions.

Regression Analysis

Weight was a significant positive factor for controls and duodenal ulcer sufferers in both countries (Table 2). Age, by itself or together with weight, was a significant negative factor in the U.K. controls, but not in the Sudanese controls.

TABLE 1. *Summary of data for duodenal ulcer and control groups.*

Study groups	Mean ± SD	Control	Duodenal ulcer
NUMBERS			
U.K.			
Women	--	44	52
Men	--	78	143
Sudan			
Women	--	17	8
Men	--	37	38
WEIGHT (kg)			
U.K.			
Women	$\bar{x}$	56.9	57.4
	s	11.3	10.9
Men	$\bar{x}$	70.4	68.8
	s	10.3	12.5
Sudan			
Women	$\bar{x}$	57.9	46.1
	s	15.9	5.9
Men	$\bar{x}$	59.6	62.2
		8.8	12.1
AGE (yr)			
U.K.			
Women	$\bar{x}$	47.7	46.4
	s	16.7	15.3
Men	$\bar{x}$	40.1	45.0
	s	15.3	13.4
Sudan			
Women	$\bar{x}$	32.2	25.1
	s	15.1	9.1
Men	$\bar{x}$	31.4	33.8
	s	14.2	9.7

$\bar{x}$ = sample mean; s = sample standard deviation.

Initially, therefore, the subjects of each country were standardized to their respective mean weights.

TABLE 2. *Single and multiple regressions, maximal acid output (mmol h^{-1}).*

SUDAN

Controls (N = 54)

(1) $MAO = 0.24*Weight + 5.05, r = 0.31, P < 0.02$

Duodenal ulcer (N = 46)

(2) $MAO = 0.30*Weight + 11.27, r = 0.31, P < 0.02$

UNITED KINGDOM

Control (N = 122)

(3) $MAO = 0.38*Weight + 1.05, r = 0.37, P < 0.001$

(4) $MAO = 0.33*Weight - 0.26*Age + 15.31, r = 0.49, P < 0.001$

Duodenal ulcer (N = 195)

(5) $MAO = 0.33*Weight + 14.26, r = 0.27, P < 0.001$

MAO = maximal acid output.

TABLE 3. *Standardized maximal acid output (to mean nationality weight).*

Study groups	Mean ± SD	Control	Duodenal ulcer	
UNITED KINGDOM				
Females	$\bar{x}$	22.7	29.5	$t = 3.7$
	s	7.2	10.7	$P = 0.001$
Males	$\bar{x}$	27.2	37.8	$t = 5.3$
	s	13.7	14.8	$P < 0.001$
		$t = 2.4$ $P < 0.02$	$t = 4.3$ $P < 0.001$	
SUDAN				
Females	$\bar{x}$	17.9	19.5	$t = 1.0$
	s	9.1	7.4	N.S.
Males	$\bar{x}$	21.2	30.3	$t = 3.9$
	s	9.3	10.7	$P < 0.001$
		$t = 1.2$ N.S.	$t = 2.8$ $P < 0.01$	

$\bar{x}$ = sample mean; s = sample standard deviation;
N.S. = not significant.

Weight Standardization

By using Equation 3 of Table 2, the U.K. controls were standardized to a weight of 65 kg. Similarly, the U.K. patients with duodenal ulcer were standardized to 65 kg using Equation 5. After standardization, the differences between men and women as well as controls and duodenal ulcer patients in the U.K. group were significant at $P < 0.02$ (Table 3). Since there was not much difference in the mean ages of the subgroups in the U.K. group, and the effect of weight had been removed by standardization, these differences were apparently not due to the effect of weight or age.

Using Equations 1 and 2 of Table 2, both the Sudanese control and duodenal ulcer subjects were standardized to 58 kg (the mean weight of the Sudanese controls) by their respective equations. When this was done, the male duodenal ulcer patients differed significantly from both the female patients with duodenal ulcer and the male controls ($P < 0.01$) (Table 3). Again, these differences could not be attributed to the small differences in age.

Standardization for Nationality

By using Equations 4 and 5 of the U.K. data, the subgroups of the U.K. data could be standardized to the weight (and in the case of the controls, to the age) of their respective Sudanese subgroup (Table 4). When this was done, the small difference between the Sudanese and U.K. female controls remained nonsignificant. However, there was a between-country difference shown by the male controls ($P < 0.01$) that was not due to weight or age. This conclusion also holds true for the significant difference between the male subjects with duodenal ulcer ($P < 0.02$). The U.K. females with duodenal ulcer did not differ from their Sudanese counterparts, but their mean ages were dissimilar (46 and 25 years, respectively). A correction for age, were it possible, would have increased the difference in their maximal acid output.

TABLE 4. *MAO standardized to weight (and age, for the controls) of their Sudanese counterparts.*

Groups		Control			Duodenal ulcer		
		U.K.	Sudan		U.K.	Sudan	
Female	$\bar{x}$	20.1	17.9	$t = 0.9$	22.8	17.9	$t = 1.4$
	s	7.2	9.1	N.S.	10.7	8.8	N.S.
Males	$\bar{x}$	28.1	21.2	$t = 3.2$	36.7	31.5	$t = 2.5$
	s	13.1	9.3	$P < 0.002$	14.8	10.4	$P < 0.02$

MAO = maximal acid output.

The Effect of Chronic Smoking

The percentage of smokers in each of the eight subgroups was plotted against the weight-standardized maximal gastric secretion. The results show a distinct trend for the U.K. series, with the gastric output increasing with the percentage of smokers (Figure 1). The male Sudanese subjects with duodenal ulcer who were also smokers showed the same tendency and were the only Sudanese subgroup to show raised gastric secretion.

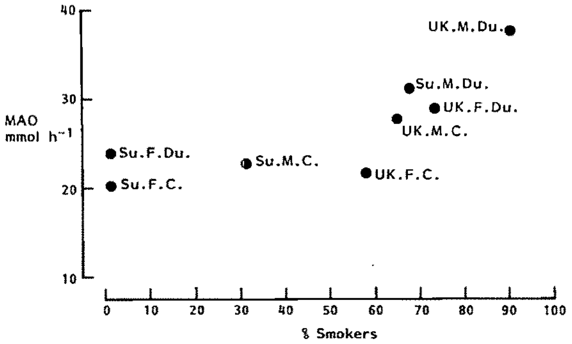

FIGURE 1. The relationship of maximal gastric secretion to the percentage of smokers in each subgroup. (*Su* = Sudan; *UK* = United Kingdom; *M* = male; *F* = female; *C* = control; *Du* = duodenal ulcer.)

Discussion

The U.K. series is part of a continuing study, with diagnosis of duodenal ulcer made by endoscopy or at operation, and the smoking history of subjects carefully checked for lapsed nonsmokers. The Sudanese series is a one-off project, with diagnosis based on symptoms and radiological findings. All females were assumed to be nonsmokers. These differences in method, together with the fact that the U.K. group is larger, allows the U.K. series, in some respects, to serve as a model to which the Sudanese series could be compared.

The sex difference observed in Westerners is thought to be due to the influence of stature (e.g., weight, lean body mass, height), as has been found in some European studies[6,7,15] as well as in a study conducted in India.[1] Correction for stature has been shown to eliminate the difference in maximal gastric secretion between the sexes in both control and duodenal ulcer groups.[7] After such correction, significant differences, within the duodenal ulcer or control groups and within the same sex, still persist between Westerners and non-Westerners.[4] However, the method of standardizing used in this study by Lam et al[4] (i.e., expressing secretion per kilogram) was probably invalid since the intercept of the regression of secretion against weight appears to be significantly different from zero.

In the present series, the U.K. controls exhibited a significant effect of age, even after weight had been taken into account (Equation 4, Table 2). In the Sudanese controls, however, only the effect of weight was discernible in the regression analysis. This lack of a correlation with age may be due to the smaller numbers of subjects in the Sudanese group or the more limited age range. The Sudanese, in general, were much younger than the U.K. subjects. For instance, the female Sudanese duodenal ulcer sufferers started showing their ulcer symptoms at the average age of 21 whereas for their U.K. counterparts this age was 36.

In previous studies of the U.K. data, we have standardized for the stature of the subjects by using a regression line based on height.[14] In the present study, weight was used, because in the Sudanese controls no significant correlation between height and maximal gastric secretion was found. Again, this was probably due to the small sample size.

Therefore, using weight (and in controls, age) to standardize between the nationalities, the maximal gastric secretion of Sudanese men was significantly less than that of U.K. men for both controls and subjects with duodenal ulcer, while the secretion rates for women did not differ.

Peptic ulcer in the Sudan is an uncommon disease. In 1974, the reported incidence was 0.001%.[16] While this may be an underestimate, a more pertinent finding was the male to female ratio in the middle-age group (25 to 44 years) of peptic ulcer sufferers which was 25:1. The earlier and older groups had an overall ratio of 1.4:1.

It is difficult to reconcile the possible effects of diet with these epidemiological findings, and of race with our findings on the gastric secretion rates in Sudanese with duodenal ulcer, since both factors should affect the sexes equally. However, they are compatible with a sex-related genetic effect or a sex-related environmental effect such as smoking.

In the present study, the percentage of smokers in each subgroup was plotted against their weight-standardized maximal gastric secretion. A trend was noted for both sexes in the U.K. group (Figure 1), but for only male subjects with duodenal ulcers in the Sudanese group.

There have been several papers[6-10] describing a long-term effect of cigarette smoking on maximal gastric secretion and this appears to operate in both control and duodenal ulcer subjects. Our finding in the present study that maximal gastric secretion tends to increase with increasing percentage of smokers in the population is in agreement with these results. It has also been reported[17] that, of a sample of adult Australians with duodenal ulcer, 55% were smokers but only 22% of the matched community controls were smokers.

It is conceivable, therefore, that Figure 1 shows the existence of at least two factors leading to duodenal ulcer: the first, found in the Sudanese females with duodenal ulcer, does not operate by means of raised gastric secretion, but may be associated with their early age of onset, and the second, found in the remaining duodenal ulcer subgroups, operates through the effect of gastric secretion and is apparently associated with long-term smoking.

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HISTOLOGIC PATTERNS OF LYMPHADENOPATHY IN THE EASTERN PROVINCE OF SAUDI ARABIA

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راجعنا نتائج التشريح المرضي النسجي لألف خزعة متتالية من عقد لمفية أخذت من مرضى سعوديين وغير سعوديين. كان متوسط العمر ٣٣,٤ ± ١٧,٣ سنة، ونسبة الذكور إلى الإناث ٣ : ١ أشار تحليل البيانات إلى الموجودات التالية بالنسبة إلى التشريح المرضي النسجي: ٣٧٪ ارتكاسية، ٣٠٪ التهاب العقدة اللمفية الورمي الحبيبي، ١٤,٣٪ ورم نقيلي، ٨,٧٪ ورم لمفاوي غير هودجيكيني و ٦,٨٪ هودجكن. شكلت العقد اللمفية الرقبية أكثر المجموعات تواردا (٥٩,٦٪) بينما كانت العقد اللمفية جنيب الأبهر أقل المواقع اصابة ٢,٢٪).

We reviewed the histopathological findings in 1000 consecutive lymph node biopsy specimens obtained from both Saudi and non-Saudi patients. Mean patient age was 33.4 ± 17.03 years, with a male to female ratio of 3:1. Analysis of the data indicated the following histopathological findings: 37%, reactive; 30%, granulomatous lymphadenitis; 14.3%, metastatic neoplasm; 8.7, non-Hodgkin's lymphoma; and 6.8%, Hodgkin's disease. The cervical lymph nodes constituted the most common group (59.6%), whereas paraaortic lymph nodes were the least common site (2.2%).

Lymphadenopathy is a common clinical manifestation of a variety of pathological conditions. There are several causes of lymphadenopathy—these include inflammatory conditions such as reactive non-specific hyperplasia; specific bacterial infection such as tuberculosis, leprosy, syphilis, or brucellosis; and viral lymphadenopathy.[1-7] It can also be caused by certain immunological disorders such as rheumatoid arthritis and angioimmunoblastic lymphadenopathy.[8-10] Enlargement of lymph nodes can also be due to partial or complete replacement by metastatic neoplasms, and this is the most common finding reported from other studies.[11]

Although lymphadenopathy is commonly encountered in Saudi Arabia, reports are sporadic and surveys are mostly confined to either cases of primary neoplasm or of certain inflammatory conditions that are limited to certain sites.[12-17] Our report describes the histopathological pattern of lymphadenopathy in Saudi Arabia, including our initial data depicting the spectrum of the condition in our study population.

Material and Methods

A total of one thousand consecutive lymph node specimens that had been removed surgically and undergone histopathological examination between 1981 and 1988 were retrieved from the files of the histopathology laboratory at King Fahd Hospital of the University (KFHU), Al-Khobar. These specimens had been obtained from patients seen at KFHS and the private hospitals in the Dammam, Al-Khobar, region. Lymph nodes removed as part of radical cancer resection in previously diagnosed cases were excluded. Specimens were fixed in formalin and embedded in paraffin. Routine hematoxylin-eosin staining

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was done on all, with special staining as required. These special stains included periodic acid–Schiff, Ziehl-Neelsen, reticulin, and methyl green–pyronine. All sections were examined by the three pathologists. The clinical information obtained from the patient charts included age, sex, nationality, and location of lymphadenopathy.

A computerized data base was constructed to store the available core data, and simplified scheme for diagnosis was adopted. Comparison of proportion was carried out using the chi-square test. The two-tailed *t* test without correction for multiple comparison was used to test differences in mean age among various diagnostic groups. $P < 0.05$ was considered significant and all significances reported are two-tailed. All statistical analyses were carried out using the BMDP statistical software package.

Results

Of the one thousand cases reviewed, 65% were in Saudis and 35% in non-Saudis, for a ratio of 2:1. Mean patient age was 33.4 ± 17.03 years (SD); age ranged from 1 to 85 years (Figure 1). The male-to-female ratio was approximately 3:1. The histopathological pattern of lymphadenopathy in relation to nationality is demonstrated in Table 1.

Of the total cases, 387 (38.7%) lymph nodes showed dilated sinusoids filled with macrophages in both cortical and medullary areas, with proliferation of mature lymphoid follicles and expansion of the paracortical zone, and these were considered reactive (Figure 2, Table 2). In 300 (30%) lymph nodes, the architecture was completely or partially effaced by a proliferation of epithelioid and caseating granuloma along with the presence of Langhan's giant cells. Ziehl-Neelsen staining was positive for acid-fast bacilli in approximately 10% of the cases examined. These were considered granulomatous lymphadenitis, of which 66 were noncaseating granuloma and 234 caseating. In 87 cases, the node architecture was completely effaced by neoplastic lymphoid cells. These were subclassified, according to the working formulation and using only a conventional stain, into the following: 27 (31%) low grade, 31 (36%) intermediate, and 29 (33%) high grade. Sixty-eight lymph node specimens showed complete loss of architecture and infiltration of eosinophils and other inflammatory cells, with the presence of Reed-Sternberg or lacunar cells. These were evaluated according to Reye's classification, with the following breakdown: lymphocyte predomin-

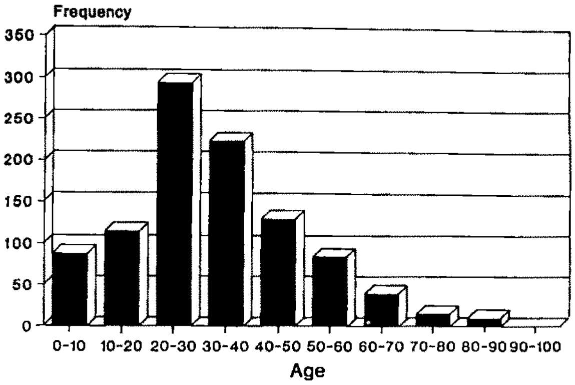

FIGURE 1. Incidence of lymphadenopathy distributed according to age.

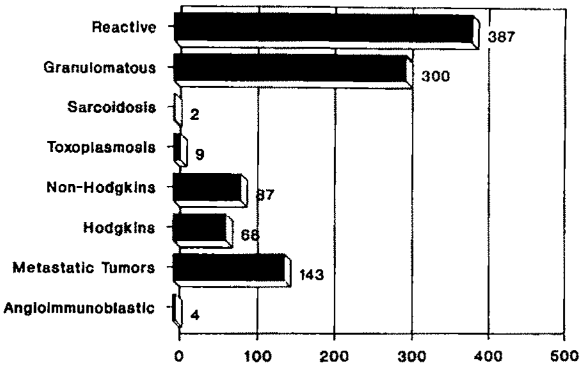

FIGURE 2. Histological patterns of lymphadenopathy in 1000 cases.

TABLE 1. *Histological diagnosis in relation to nationality in 1000 consecutive specimens studied.*

Diagnosis	Saudi	Non-Saudi	Both
Reactive	252 (38.7%)	135 (38.5%)	387 (38.7%)
Granulomatous	183 (28.1%)	117 (33.4%)	300 (30.0%)
Sarcoidosis	2 (0.3%)	0	2 (0.2%)
Toxoplasmosis	7 (1.1%)	2 (0.6%)	9 (0.9%)
Non-Hodgkin's lymphoma	58 (8.9%)	29 (8.3%)	87 (8.7%)
Hodgkin's disease	50 (7.7%)	18 (5.1%)	68 (6.8%)
Metastatic neoplasm	98 (15.1%)	45 (12.9%)	143 (14.3%)
Angioimmunoblastic lymphadenopathy	0	4 (1.1%)	4 (0.4%)
Total	650	250	1000

ant, 13 cases; lymphocyte depleted, six cases; mixed cellularity, 34 cases; and nodular sclerosis, 15 cases.

In 143 cases, the lymph nodes were completely or partially replaced by carcinomatous or sarcomatous infiltrate. Cervical and axillary lymph nodes were the most common site for metastasis. Moreover, nine lymph nodes showed marked follicular hyperplasia with dilatation of the sinusoids, which were filled with monocytoid cells. There were clusters of epithelioid cells in the parenchyma. Serological testing confirmed toxoplasmosis in these cases. Four cases also showed vascular proliferation with the marked presence of immunoblasts admixed with eosinophils where the architecture was completely obliterated. These cases were considered as angioimmunoblastic lymphadenopathy. Two cases, which showed noncaseating granuloma with asteroid bodies associated with other systemic lymphadenopathy and a positive Kveim test, were considered sarcoidosis.

In assessing histological diagnosis in relation to nationality, it was found that Saudis and non-Saudis exhibit a similar distribution of cases (Table 1). The breakdown of cases according to site is shown in Table 2. Most cases of lymphadenopathy were cervical (N = 596), followed by mesenteric (N = 123) and axillary (N = 113); the paraaortic nodes were the least frequent site (N = 22).

Comparison of the mean age of patients with various histological diagnoses is shown in Table 3, along with the *P* values. Obvious statistically significant differences were observed in those patients with reactive lymphadenopathy, with granulomatous lymphadenitis, and with Hodgkin's disease and lymphadenopathy caused by non-Hodgkin's lymphoma and metastatic carcinoma. This last disease tends to occur in the older subjects. No differences in the mean age were noted between patients with reactive lymphadenopathy, tuberculosis, and Hodgkin's dis-

TABLE 2. *Histological diagnosis relative to site of lymphadenopathy in 1000 consecutive patients.*

Diagnosis	Cervical	Axillary	Mediastinal	Para-aortic	Mesenteric	Groin	Porta Hepatis	Total
Reactive	180 (30.2)	43 (38)	13 (52)	6 (27.2)	59 (48)	60 (68.2)	26 (79)	387 (38.7)
Granulomatous	249 (41.8)	26 (23)	4 (16)	1 (4.5)	12 (9.8)	4 (4.5)	4 (12)	300 (30.0)
Sarcoidosis	2 (0.3)	0	0	0	0	0	0	2 (0.2)
Toxoplasmosis	8 (1.3)	1 (0.9)	0	0	0	0	0	9 (0.9)
Non-Hodgkin's lymphoma	46 (7.7)	4 (3.5)	0	8 (36.4)	16 (13.0)	12 (13.6)	1 (3)	87 (8.7)
Hodgkin's disease	49 (8.2)	6 (5.3)	0	2 (9.0)	5 (4.1)	6 (6.8)	0	68 (6.8)
Metastatic	61 (10.2)	33 (29.2)	7 (28)	5 (22.7)	31 (25.2)	4 (4.5)	2 (6)	143 (14.3)
Angioimmunoblastic lymphadenopathy	1 (0.2)	0	1 (4)	0	0	2 (2.3)	0	4 (0.4)
Total	596	113	25	22	123	88	33	1000

Numbers in parentheses are percentages.

TABLE 3. *Comparison of the mean age of patients with various histological diagnoses.*

Group	Mean ± SD	Group	Mean ± SD	*P* value
Reactive	29.9 ± 17.2	Granulomatous	30.7 ± 12.5	0.48
Reactive	29.9 ± 17.2	NHL	38.4 ± 20.4	0.0001
Reactive	29.9 ± 17.2	HD	28.2 ± 12.6	0.45
Reactive	29.9 ± 17.2	Carcinoma	46.2 ± 17.0	< 0.0001
Granulomatous	30.7 ± 12.5	NHL	38.4 ± 20.4	< 0.0001
Granulomatous	30.7 ± 12.5	HD	28.2 ± 12.6	0.136
Granulomatous	30.7 ± 12.5	Metastatic carcinoma	46.2 ± 17.0	< 0.0001
NHL	38.4 ± 20.4	HD	28.2 ± 12.6	0.0004
NHL	38.4 ± 20.4	Carcinoma	46.2 ± 17.0	0.0016
HD	28.2 ± 12.6	Carcinoma	46.2 ± 17.0	0.0016

NHL = non-Hodgkin's lymphoma; HD = Hodgkin's disease.

ease since all these diseases occur in younger patients.

Discussion

Lymphadenopathy as a primary presenting sign poses a common diagnostic problem for both physicians and surgeons, as it raises the possibility of primary or secondary malignancy, particularly when it is firm, multiple, and painless. Histopathological study is especially effective in establishing diagnosis, as systemic symptoms, such as fever, weight loss, or malaise, frequently are not present. In addition, routine laboratory investigations often fail to reveal an answer.

This retrospective study identifies various histopathological patterns of lymphadenopathy as seen in the inhabitants of the Eastern province. Reactive hyperplasia, which represents a reactive process to various antigenic stimuli, is the most common, and this agrees with other observations from Saudi Arabia[16] and from elsewhere in the world.[18,19] Granulomatous lymphadenitis is the next in frequency and angioimmunoblastic lymphadenopathy is the last in frequency (Table 2).

Granulomatous lymphadenitis accounts for approximately one third of the cases in this study, and consists of both caseating and noncaseating types. Lymphadenitis can result from a variety of causes, including bacteriologic, immunologic, viral, and environmental. Tuberculosis and brucellosis are common infectious diseases in Saudi Arabia.[20,21] Tuberculosis has been found to account for 54.5% of the cases of peripheral lymphadenitis.[22] Acid-fast bacilli and other atypical mycobacteria are best demonstrated by culture because the histopathological yield using the Ziehl-Neelsen stain is only 10%.[1] Sarcoidosis was found in only two cases of granulomatous lymphadenitis, which was also confirmed by other clinical and laboratory investigations. Sarcoidosis is considered rare in Saudi Arabia and other Middle Eastern countries,[23,24] though recent findings reported from Jordan show that it is not as rare as it was thought to be.[25] Therefore, most of the cases of granulomatous lymphadenitis encountered in our study must be tuberculous in origin, though other causes should be considered.

Neoplastic lymphadenopathy is found in approximately 30% of cases. Primary lymph node neoplasm, i.e., Hodgkin's disease and non-Hodgkin's lymphoma, constitutes more than 50% of these cases, with metastatic carcinoma or sarcoma accounting for the remainder. Hodgkin's disease constituted 48.8% of all the primary neoplasms, in agreement with the statistics reported for other countries,[26-30] though higher than earlier findings in Saudi Arabia.[31] Mixed cellularity was the most common type, and this is the finding for other developing countries[30-35] but is in contrast to that reported for developed countries where the nodular sclerosis is the most common type.[36,37] Non-Hodgkin's lymphoma was a relatively common finding in our study. Intermediate grade is the most common type, and this is the observation for both Saudi Arabia and elsewhere.[15,38-40] Angioimmunoblastic lymphadenopathy, a lymphoma-like syndrome first described in 1974,[41] is the least common. It can occur in a generalized form, and rarely in a local form, with variable life expectancy ranging from two months to four years. This disease has a tendency to transform into malignant lymphoma.[42]

Our study reveals that the most commonly enlarged and biopsied lymph nodes are cervical, and this correlates with other reports.[16,17] The cervical lymph nodes also possess the best diagnostic features, compared to inguinal or axillary nodes.[18,43] The least common site of involvement is mesenteric, accounting for only 2.2% of the cases. Supraclavicular lymph nodes have, in particular, the best diagnostic yield of all peripheral lymph nodes with an 85.2 to 90% yield.[43]

Our study highlights the common cause of lymphadenopathy in Saudi Arabia where almost 70% of the cases are found to be inflammatory, in contrast to the 60% predominance of neoplastic cases reported elsewhere.[11] Granulomatous lymphadenitis is still a common cause of lymphadenopathy in this country, in both Saudi and expatriate populations. Lymph node biopsy remains an important aid in the investigation and management of these patients.

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CLINICAL FEATURES AND RESULTS OF TREATMENT OF HODGKIN'S DISEASE IN PRE-SCHOOL SAUDI CHILDREN

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كان هدف هذه الدراسة تحليل السمات السريرية ونتائج معالجة الأطفال السعوديين، دون سن المدرسة (أقل من ست سنوات)، والمصابين بداء هودجكن بلغ عدد المرضى ٣٤ مريضًا (٢٨ ذكرًا و ٦ اناث، النسبة ٤,٧ : ١) راجعوا مستشفى الملك فيصل التخصصي ومركز الأبحاث على مدار ١٤عامًا (١٩٧٥م - ١٩٨٩م). تراوح معدل العمر إبان القدوم إلى المستشفى بين ١٨ و ٦٦ شهرا (المتوسط ٤٢ شهرا). وقد تضمنت الشكاوي آنذاك ضخامة العقد اللمفاوية لدى ٣٣ مريضًا، وفقر الدم لدى ١٥مريضًا وحمى لدى ١٣ مريضًا. كانت الأنماط النسيجية كما يلي: مختلط الخلايا لدى ٢٢ مريضًا (٦٥٪)، والتصلب العقيدي لدى ١٠ مرضى (٢٩٪) المرحلة الثالثة: خمسة عشر مريضًا (٤٤٪) والمرحلة الرابعة: ثلاثة مرضى (٩٪). خضع تسعة وعشرون مريضا للمعالجة الكيميائية وتلقى أربعة مرضى فقط معالجة شعاعية بينما تلقى مريض واحد كلتا المعالجتين. عاش تسعة عشر مريضًا (٥٦٪) خالين من المرض من ٨ - ١٣٥ شهرا (المتوسط ٤٨ شهرا)، وانتكست حالات أربعة مرضى فخضعوا لعلاج بديل، وتوفي مريضان وغاب تسعة مرضى عن مراجعة المستشفى. كان داء هودجكن لدى الأطفال في هذه الدراسة يميل نحو المراحل المتقدمة عند التشخيص وكان نمط الخلايا المختلطة هو الغالب. وقد تحمل المرضى أساليب المعالجة دون حدوث آثار جانبية خطيرة وكانت الاستجابة للعلاج جيدة بشكل عام.

The purpose of this study was to analyze the clinical features of and results of treatment in pre-school Saudi children (< 6 years of age) with Hodgkin's disease. The subjects were 34 patients (28 boys and 6 girls; male to female ratio, 4.7:1) seen at King Faisal Specialist Hospital and Research Centre (KFSH&RC) over a period of 14 years (1975 to 1989). The age range at the time of presentation was 18 to 66 months (median, 42). Presenting complaints included lymphadenopathy in 33 patients, anemia in 15, and fever in 13. Histological subtypes included mixed cellularity in 22 patients (65%), nodular sclerosis in ten (29%), and lymphocyte depletion and lymphocyte predominance in one patient each (2.9%). The distribution of the patients among the clinical stages at presentation was as follows: Stage I, six patients (18%); Stage II, ten patients (29%); Stage III, 15 patients (44%); and Stage IV, three patients (9%). Twenty-nine patients underwent chemotherapy and only four patients had radiotherapy; one patient received both. Nineteen patients (56%) survived disease-free from 8 to 135 months (median, 48 months), four suffered relapse and underwent alternate therapy, two died, and nine were lost to follow-up. The childhood Hodgkin's disease in pre-school children seen in our study tended to be more advanced at diagnosis and the mixed cellularity form was predominant. The methods of treatment were tolerated without serious side effects and the overall therapeutic response was good.

Hodgkin's disease is rarely seen in children younger than 6 years in Western countries, and therefore, very little is known about the clinical behavior of the disease in this age group. This report describes our findings in children treated at King Faisal Specialist Hospital and Research Centre (KFSH&RC) from 1975 until 1989. To our

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knowledge there are no similar series reported in the world literature.

Methods and Patients

The hospital medical records of all children younger than 6 years who had Hodgkin's disease and who were seen at KFSH&RC between 1975 and 1989 were reviewed for age, sex, clinical presentation, histological subtype, stage, treatment, and outcome of therapy. Diagnosis was always based on the histological findings in tissue biopsy specimens obtained either at KFSH&RC or referring institutions. When biopsies were performed outside our institution, slides were reviewed and reported on by one of the institution's pathologists. The duration of clinical signs and symptoms at the onset of the disease until referral to KFSH&RC ranged from 2 to 30 months (median, 8). Clinical staging was carried out in 26 children and surgical staging, which included exploratory laparotomy with lymph node biopsy and splenectomy, was done in the remaining eight.

Initial evaluation for all patients included physical examination, blood chemistry, bone marrow aspiration and biopsy, chest radiography, and sonography of the abdomen. Computed tomography, liver and spleen scans, bone scans, and other modalities of radiological imaging were done when indicated.

The treatment protocol called for radiotherapy only in patients with Stage IA disease and this affected only four patients. One additional patient received radiation and chemotherapy. Chemotherapy was given to all other patients. The chemotherapy included mechlorethamine, vincristine, procarbazine, prednisone (MOPP) (24 patients), MOPP + adriamycin, bleomycin, vinblastine, dacorbazine (ABVD) (4 patients), and chlorambucil, vinblastine, procarbazine, prednisone (CHIVPP) + ABVD (one patient). Most patients were followed closely and seen at scheduled intervals. A small number of patients were routinely evaluated at referral hospitals.

Results

One hundred sixty-eight children with Hodgkin's disease were treated at KFSH&RC from 1975 until 1989. Of these, 34 (20%) were younger than 6 years (< 3 years, 15 patients; 3 and 4 years, seven; and 5 and 6 years, 12). There were 28 boys and six girls (male to female ratio, 4.7:1) (Table 1, Figure 1). These 34 children comprised the study population.

TABLE 1. *Relationship between ages and clinical stages.*

Age group in months	Stage I	Stage II	Stage III	Stage IV
12–24	2	1	0	0
25–36	3	2	5	2
37–48	0	3	4	0
49–72	1	4	6	1
Total	6	10	15	3

TABLE 2. *Initial clinical presentation.*

Clinical presentation	No. of patients	Primary sites of involvement	No.
Lymphadenopathy	33 (97%)	Left cervical lymph node	17
B symptoms	13 (38%)	Right cervical lymph node	16
Hepatomegaly*	8 (23%)	Lower abdomen	1
Splenomegaly	6 (18%)		

* Three patients had Stage IV disease. The other five had borderline enlargement, but liver enzyme and ultrasound findings were normal.

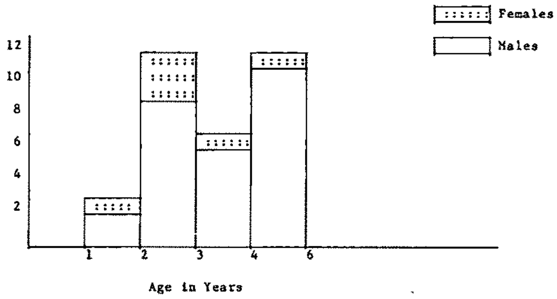

FIGURE 1. Distribution according to age and sex at diagnosis.

The most common presenting features in these patients were painless swelling of the lymph nodes, hepatosplenomegaly, and constitutional symptoms (Table 2). None of the children had bone marrow involvement.

Twenty-eight patients underwent clinical staging and six surgical staging: six were in Stage I, ten in Stage II, 15 in Stage III, and three in Stage IV. There was no significant correlation between the histological subtype and stage of the disease (Table 1).

The histological subtypes were as follows: 22 patients (65%) had mixed cellularity, ten (29%)

had nodular sclerosis, one (3%) had lymphocyte predominance, and one (3%) had lymphocyte depletion.

The outcome of treatment is summarized in Table 3. Twenty-five children received MOPP therapy. Of these, three suffered relapse, one died from pneumonia after one course of therapy, six were lost to follow-up while in remission, and 15 enjoyed continuous complete remission for 24 to 112 months (median, 53). Four patients received radiotherapy only. Of these, one patient suffered relapse, one was lost to follow-up while in remission, and two have been in continuous complete remission for 36 and 135 months. Four additional patients received MOPP and ABVD chemotherapy. Of these, one child died who did not respond to chemotherapy, one was lost to follow-up while in remission, and two are in continuous complete remission. One child received MOPP chemotherapy and radiotherapy but was lost to follow-up. Table 4 summarizes the pathological and clinical characteristics of those patients who died early or suffered relapse.

TABLE 3. *Treatment outcome.*

Outcome	MOPP	MOPP + ABVD	MOPP + RT	RT
CCR	15	2	–	2
Died	1	1	–	–
Relapsed	3	0	–	1
LFU	6	1	1	1
Total	25	4	1	4

MOPP = mechlorethamine, vincristine, procarbazine, prednisone; ABVD = adriamycin, bleomycin, vinblastine, dacarbazine; RT = radiotherapy; CCR = continuous complete remission; LFU = lost to follow-up.

Discussion

The geographical variation seen in association with the incidence and clinical behavior of lymphomas in children has been well documented.[1-4] This is particularly true for Hodgkin's lymphoma which in developing countries is seen in higher relative frequency and in younger age groups. The mixed cellularity type is also more commonly seen in developing countries.[5-9]

Very little has been published about the clinical behavior of the disease in the very young (i.e., those under 6 years of age). In fact, there appears to be no report dealing specifically with pre-school children considered as a separate group.[10] Nearly 20% of the children afflicted with Hodgkin's disease who have been seen at KFSH&RC were below 6 years of age.[11] This finding is more striking if considered in terms of the child's age when signs and symptoms were observed by the parents. It usually took between 2 and 30 months (median, 8) before patients were referred to KFSH&RC.

Late-stage Hodgkin's disease also predominates, but this could be due to the fact that our patients may be referred late, the disease may be more aggressive in this age group, or both. This could also account for the predominance of the mixed cellularity type. It is not clear whether the mixed cellularity is an evolution from other types (lymphocyte predominance and nodular sclerosis)

TABLE 4. *Clinical and pathological characteristics of patients who died early or relapsed.*

Patient no.	Age (yr)	Sex	Stage	Histology	Initial state of presentation	Treatment	State of relapse	Duration of remission (mo)	Treatment of relapse	Outcome
1	3	M	IIB	MC	Left cervical	1 course MOPP	None	3	Pneumonia	Dead
2	3.4	M	IIB	MC	Right cervical	6 MOPP	Liver	45	ABVD	Alive
3	5	M	IIA	MC	Abdominal mass	6 ChlVPP	Abdominal mass	16	ABVD	Alive
4	3.6	M	IIIB	NS	Splenomegaly	6 MOPP	Spleen	18	ABVD	Alive
5	3	M	IA	NS	Right cervical	Radiotherapy	Liver	30	MOPP	Alive
6	5	M	IVB	LD	Left cervical	5 MOPP/ 4 ABVD	None	11	Pneumonia	Dead

MC = mixed cell; NS = nodular sclerosis; LD = lymphocyte depletion; MOPP = mechlorethamine, vincristine, procarbazine, prednisone; ABVD = adriamycin, bleomycin, vinblastine, dacarbazine; ChlVPP = chlorambucil, vinblastine, procarbazine, prednisolone; M = male; F = female.

or is a characteristic of Hodgkin's disease in young children.[6] The presenting features and the sites of involvement, however, appear to be similar to those observed in other pediatric age groups.

Surgical staging (laparotomy with splenectomy and lymph node biopsy) has been avoided as much as possible because of the hazards of splenectomy in this age group.[12,13] It is likely that in our series most of the Stage I and II cases were actually in Stage III. A previous study[13] demonstrated that half of our patients in clinical Stage I disease and all in clinical Stage II were actually in Stage III, based on findings at surgical staging. For this reason and because of the possible postradiation sequelae in young children, cyclic combination therapy was the principal mode of treatment in these children.

The remission rate following treatment has been significant; only one child who received an adequate trial of chemotherapy failed to go into remission. Since late recurrences in Hodgkin's disease are known to happen after a more extended period, longer follow-ups are needed before complete cure can be assured. Our results compare well with those in other series in which chemotherapy and/or radiotherapy were used to treat older children with Hodgkin's disease.[14] A major concern relates to the development of secondary malignancies in patients who receive different combined modalities of treatment.[15,16] Thus far, none of our patients have had such an occurrence. Another well-justified concern is the possibility of infertility secondary to MOPP therapy. Most of the patients in our series are still too young to be evaluated for this. Even though Hodgkin's disease appears to develop at a younger age in our patient population, and this is compounded by delays in referral for appropriate treatment, these pre-school children tolerate therapy well and their response to treatment is as good as that observed in older children.

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GUAR GUM IN NON-INSULIN-DEPENDENT DIABETES MELLITUS: A DOUBLE-BLIND CROSSOVER, PLACEBO-CONTROLLED TRIAL IN SAUDI ARABIAN PATIENTS

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اجرينا تجربة مزدوجة الإغفال ومتبادلة ومضبوطة باستخدام الغُفل وذلك لتقييم أثر اضافة الصمغ الهندي النباتي (غُوار) مع الطعام في السيطرة على سكر الدم وتركيز شحوم الدم ووزن الجسم لدى ٣٩ من السعوديين المصابين بداء السكري غير المعتمد على الإنسولين. كان جميع المرضى يعانون من السمنة وإخفاق الحمية مع الجرعات القصوى من خافضات السكر بالفم في السيطرة على السكري. انخفض متوسط تركيزات غلوكوز الدم حالة الصيام وغليكوزيل الهيموغلوبين بعد المعالجة بـ «الصمغ الهندي» بصورة هامة مقارنة بما كان عليه لدى مجموعة استخدام الغُفل (غلوكوز الدم حالة الصيام: ١١,٠٠ ± ٠,٤٢ مقابل ١٢,٧٠ ± ٪,٣٠ ، ٠,٥٣ ميلي مول/لتر، (P < ٠,٠١ ، ٠، غليكوزيل الهيموغلوبين ١١,٠٠ ± ٠,٣٥٪ مقابل ١١,٩٠ ± ٠,٣٠٪ P < ٠,٠٥٪). كما انخفض مستوى غلوكوز الدم بعد الأكل بشكل هام لدى إضافة الصمغ الهندي مقارنة بعدم انخفاضه لدى استخدام الغُفل مع وجبة مماثلة (P < ٠,٠٢٪) وانخفض مستوى اجمالي كولستيرول الدم من ٥,٧٦ ± ٠,٢١ ميلي مول/لتر قبل المعالجة إلى ٥,٠٠ ± ٠,١٦ ميلي مول/لتر (P < ٠,٠١٪) عند نهاية المعالجة. لم يكن هناك أي تغيير ملموس في وزن الجسم خلال مرحلتي الدراسة. ترافقت المعالجة بالصمغ الهندي في دراستنا هذه بنسبة أكبر من الأثار الجانبية مقارنة بما سبق نشره، لكن هذه النسبة انخفضت مع مرور الوقت وتحمل المرضى العقار بصورة جيدة، وجدنا في الصمغ الهندي عقارا آمنا، مفيدا وفعالا كعلاج اضافي لمعالجة المصابين بداء السكري غير المعتمد على الإنسولين والذي أخفقت المعالجة التقليدية في السيطرة عليه.

We conducted a double-blind crossover, placebo-controlled trial to evaluate the effects of guar gum, as a food additive, on glycemic control, plasma lipid concentration, and body weight in 39 Saudi patients with non-insulin-dependent diabetes mellitus. All subjects were overweight and their diabetes was uncontrolled on diet and maximum doses of oral hypoglycemic agents. Mean fasting plasma glucose (FPG) and glycosylated hemoglobin (HbA1) concentrations after treatment with guar were significantly lower than those seen with placebo (FPG: 11.00 ± 0.42 versus 12.70 ± 0.53 mmol/L; $P < 0.01$; HbA1: 11.00 ± 0.35% versus 11.90 ± 0.30%, $P < 0.05$). The postprandial plasma glucose level was also significantly lower when guar was added to an identical test meal than that observed with placebo ($P < 0.02$). The total plasma cholesterol level decreased from 5.76 ± 0.21 mmol/L prior to treatment to 5.00 ± 0.16 mmol/L ($P < 0.01$) at the end of treatment. There was no significant change in body weight during either phase of the study. Guar treatment was associated with a higher rate of side-effects in our study than have been previously reported, but this rate

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declined with time and the drug was well tolerated. We found guar to be a safe, useful, and effective adjunct in the management of patients with non-insulin-dependent diabetes mellitus that is uncontrolled with conventional therapy.

Diabetes mellitus is a major health problem in the Kingdom of Saudi Arabia[1,2] and has a high rate of complications and morbidity, especially in patients whose disease is poorly controlled.[3,6] Non-insulin-dependent diabetes (NIDD, type 2) is the predominant type in the Kingdom. When patients do not comply with their diet, are overweight, and do not exercise, maximum oral hypoglycemic therapy is usually ineffective in achieving satisfactory glycemic control. Carefully conducted studies have shown that fiber-supplemented diets improve glycemic control and decrease serum cholesterol levels in diabetics.[7,8] Viscous fiber added to the diet has been found to slow postprandial glucose absorption.[9] Of this group of nonabsorbable carbohydrates, guar has been shown to be the most effective in diminishing postprandial glycemic response, both in diabetic and nondiabetic subjects.[10,11] In addition, guar granules were shown to be more effective in lowering postprandial plasma glucose levels when simply sprinkled on the food, rather than taken as a "premeal drink."[10]

The effectiveness of guar in glycemic control, plasma lipid levels, and body weight was evaluated in overweight type 2 Saudi diabetics whose disease was not controlled by diet and maximally tolerated oral hypoglycemic agents.

Patients and Methods

Sixty-three Saudi patients with NIDD who were on oral hypoglycemic agents were recruited from the diabetes clinic at King Abdul Aziz University Hospital in Riyadh and selected according to the following criteria: (1) age, 21–70 years; (2) overweight—body mass index, > 24 kg/m; (3) treated with maximum tolerated doses of oral hypoglycemic agents for at least 6 months; (4) control of diabetes is considered moderate to poor (i.e., either FPG > 9 mmol/L or HbA1 > 10%); (5) no clinical esophageal or other gut motility dysfunction; and (6) no condition that contraindicates the use of guar.

Patients were excluded if they were pregnant or had recently undergone another drug therapy that might influence diabetic control.

Only those patients who completed both phases of the study were included in the final analysis. Thirty-nine patients completed the study. Their mean fasting plasma glucose levels during three consecutive outpatient visits before the start of the study was 12.5 ± 3.0 mmol/L. All patients were on high doses of sulfonylureas, a majority of them in combination with metformin. No change in drug therapy or diet was made in any of the patients during the study period, unless hypoglycemia occurred. Informed consent was obtained from each subject before the start of the study. Characteristics of patients completing the study are summarized in Table 1.

Study Protocol

Consecutive patients who met the inclusion criteria were allocated randomly to either a guar (Guarina; Norgine Ltd., Oxford, U.K.) treatment group or a placebo (beef gelatin) group. After 4 weeks, patients underwent a washout period of 4 weeks, then were crossed over to the opposite group and continued for 4 more weeks in a double-blind fashion. Patients were interviewed and weighed. Urine glucose, fasting plasma glucose, cholesterol, triglyceride, C-peptide, insulin, and glycosylated hemoglobin (HbA1) levels were measured, and routine biochemical and hematological determinations were done at the beginning and end of each phase of the study. Demographic data were also obtained.

Patients were asked to bring all current medications to the clinic and were issued a new two-week supply of oral hypoglycemic agents. An adequate number of packets of guar or placebo and oral hypoglycemic agents, as well as oral and written instructions for their proper use, were given to patients. One 5-gm packet of guar or placebo was to be taken with each main meal three times daily, and the guar or placebo granules sprinkled evenly over food or stirred into semisolid foods (e.g., yoghurt). Patients were told to return to the clinic every two weeks after a 10-hour fast. At each visit, body weight and urine glucose and FPG levels were determined. A medication count was also done to assess compliance. The clinical pharmacist also assessed the incidence of side-effects. An appointment for the next clinic visit plus additional medications were provided. Patients were monitored in this way throughout the entire 12 weeks of the study.

To evaluate the effect of guar gum on postprandial plasma glucose concentration, a standardized breakfast (approximately 400 calories) was provided during the second clinic visit at each study phase. Either a packet of guar or placebo was sprinkled onto the food before consumption and then the one-hour postprandial plasma glucose level was measured. The time taken to eat the breakfast was usually less than 20 minutes.

In the event that patients dropped out of the study, the reasons for this were documented.

Laboratory Assays

Plasma glucose, cholesterol, triglyceride levels, and renal and hepatic functions were estimated using a multichannel autoanalyzer (SMAC, Technicon, USA). HbA1 concentration was determined by an electrophoretic method (GLYTRAC, Corning Medical, Palo Alto, CA, USA). Plasma C-peptide and total immunoreactive insulin were assayed using commercially available radioimmunoassay kits (DRG International, NJ, USA, and Amersham, Buckinghamshire, U.K., respectively). Hematological tests were carried out using a Coulter counter.

Statistical Analysis

Since normally distributed variables were measured, Student's *t* test for paired results was used. $P < 0.05$ was considered statistically significant.

Results

Compliance, Side-effects, and Body Weight

Thirty-nine (28 females, 11 males) of 63 patients who had originally been recruited completed the study. The baseline parameters of the drop-out group were not significantly different from those in the patients who completed the study. Of the 24 patients who dropped out, 12 did so during the guar phase and 12 during the placebo phase. The main reasons for the dropout were inability to tolerate the drug in seven patients on guar and three on placebo. Eight patients failed to return, four did not comply with the drug regimen, one was admitted to the hospital for reasons unrelated to the diabetes, and one became pregnant.

TABLE 1. *Clinical data on 39 non-insulin-dependent diabetic patients.*

	Range	Mean ± SEM
Age	28–73 y	51.5 ± 1.65 y
Duration of diabetes	2–17 y	7.6 ± 0.56 y
Body weight	47.5–128 kg	76.3 ± 2.9 kg
BMI	24.6–51.3 kg/m	31.2 ± 0.98 kg/m
Fasting blood glucose	9.1–19.9 mmol/L	12.5 ± 4.96 mmol/L
HbA1	6.8–17.8%	11.4 ± 0.40%

BMI = body mass index; HbA1 = glycosylated hemoglobin; SEM = standard error of mean.

TABLE 2. *Number of patients with significant adverse effects during guar and placebo treatment.*

	Guar (N = 33)	Placebo (N = 23)
Loose stool/diarrhea	29 (87.8%)	8 (34.7%)
Flatulence	21 (63.6%)	12 (52.1%)
Abdominal cramps	4 (12.1%)	4 (17.4%)
Decreased appetite	3 (9.0%)	2 (13.0%)
Inconvenience	3 (9.0%)	2 (8.6%)
Unpalatable	2 (6.0%)	0
Nausea	2 (6.0%)	1 (4.3%)
Constipation	0	5 (21.7%)

The main side effects are listed in Table 2. Most symptoms abated after a few days of continued treatment, and in only ten patients (seven on guar and three on placebo) was the treatment discontinued because of intolerance. There was no significant change in body weight for the study entrants during either phase of the study.

Laboratory Findings

FPG and HbA1 values are shown in Table 3. The values of both at the start of each treatment period were not significantly different. The FPG level decreased significantly from 12.50 ± 0.50 mmol/L to 11.00 ± 0.42 mmol/L at the end of the guar period, while levels before and after the placebo period remained the same. The HbA1 level declined from 12.10 ± 0.42% to 11.00 ± 0.35% during the guar period, but no significant changes were observed during the placebo period. Figure 1 (A and B) shows the individual FPG and HbA1 data at the beginning and end of both treatment periods. After guar treatment, all 39 patients showed a decrease in the values of FPG and HbA1, except 11 and 10, respectively.

The concentrations of total cholesterol and triglycerides were not significantly different at the start of either study period, but there was a significant decrease in the total cholesterol level of from 5.76 ± 0.21 mmol/L to 5.00 ± 0.16 mmol/L during guar treatment but not during placebo treatment (Table 3, Figure 1C). The cholesterol concentration at the end of the guar period was significantly lower than that observed at the end of the placebo period ($P < 0.01$). There was no significant change in the mean plasma triglyceride concentration during either study period.

The one-hour postprandial plasma glucose level following guar ingestion was significantly lower than that observed following placebo treatment (14 ± 3.5 mmol/L versus 16.1 ± 3.5 mmol/L; $P < 0.02$). There was no change in the fasting plasma C-peptide and total immunoreactive insulin levels throughout the study (Table 3).

No change in any biochemical or hematological variables was observed during either phase of the study in any patient.

Discussion

Diabetes mellitus represents a major disease in

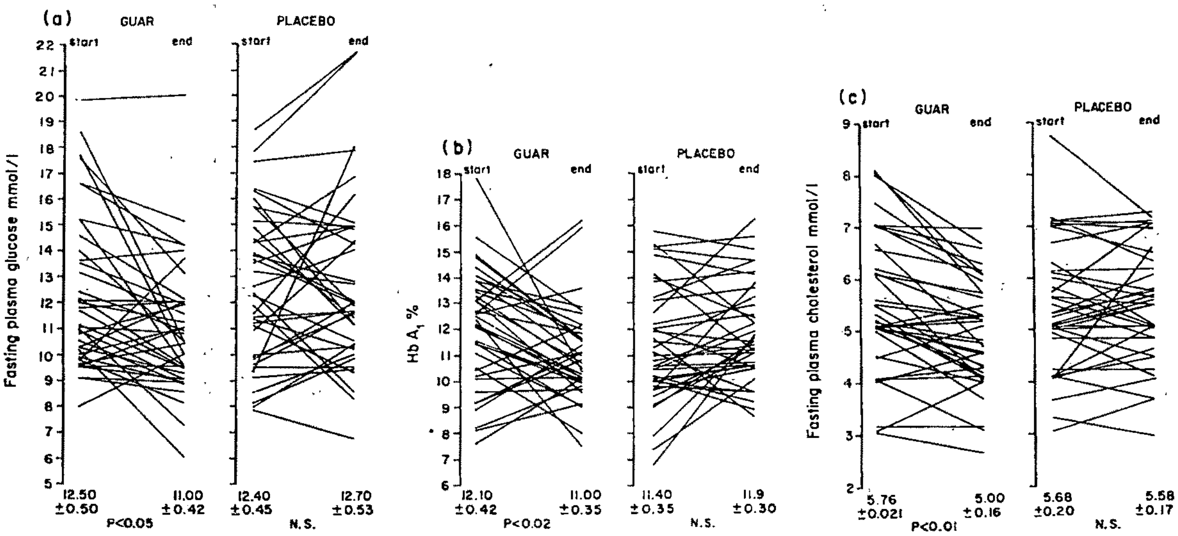

FIGURE 1. Individual changes in fasting plasma glucose (a), glycosylated hemoglobin (b), and cholesterol (c) in all 39 patients.

TABLE 3. *Clinical data on patients at the beginning and end of each treatment period.*

Clinical variables	Guar period B	Guar period E	Guar period Significance	Placebo period B	Placebo period E	Placebo period Significance
FPG (mmol/L)	12.50 ± 0.50	11.00 ± 0.42	$P < 0.05$	12.4 ± 0.45	12.7 ± 0.53	NS
HbAl (%)	12.10 ± 0.42	11.00 ± 0.35	$P < 0.02$	11.40 ± 0.35	11.90 ± 0.30	NS
Cholesterol (mmol/L)	5.76 ± 0.42	5.00 ± 0.35	$P < 0.01$	5.68 ± 0.20	5.58 ± 0.17	NS
Triglycerides (mmol/L)	2.54 ± 0.27	1.92 ± 0.20	NS	2.22 ± 0.20	2.29 ± 0.24	NS
Weight (kg)	76.00 ± 2.88	76.70 ± 2.96	NS	76.40 ± 2.90	77.1 ± 2.88	NS
C-peptide (ng/ml)	2.84 ± 0.25	2.52 ± 0.20	NS	2.53 ± 0.18	2.98 ± 0.22	NS
Insulin (m/IU/L)	32.33 ± 3.00	32.74 ± 3.10	NS	30.94 ± 3.29	29.53 ± 2.90	NS

B = beginning; E = end; FPG = fasting plasma glucose; NS = not significant; HbAl = glycosylated hemoglobin.

Saudi Arabia and predominantly occurs in the form of NIDD.[1,3] From our experience, excessive weight, diet noncompliance, and lack of exercise are the major sources of difficulty in controlling the disease in most patients, especially among females. Any adjuvant treatment is welcome in those who are inadequately managed on maximally tolerated oral hypoglycemic agents. The possible role of guar in the management of diabetes was first suggested by Jenkins et al[12] in 1976. Several later studies showed that guar gum improves both glycemic and blood lipid levels in diabetes.[10,11,13-16] Guar is a non-cellulose, soluble dietary fiber that is extracted from the cluster bean. The most effective mode of guar administration is to mix it with food.[9,13,17,18] Other modes of administration are associated with a high rate of side-effects,[17] and do not seem to be as effective.[19] For these reasons, we evaluated the use of guar in the form of granules mixed with main meals and its effectiveness in the metabolic control of patients with NIDD.

Because of the anticipated lack of compliance in keeping clinic appointments, we started with a large number of patients. Of the total 63 patients recruited, 24 dropped out (38.1%). Since equal numbers of patients dropped out during the placebo and guar phases, the high attrition rate should not affect the statistical analysis of the study results. Half of the dropouts were due to noncompliance in attending the clinics or in taking the medications as instructed.

Guar is a natural vegetable fiber that is classified chemically as a galactomannan. It has been shown to delay absorption of carbohydrates and reduce postprandial hyperglycemia and serum insulin levels.[9,10] Jenkins et al[9] demonstrated a positive correlation between the viscosity of various fibers and the mean percentage reduction of the maximum rise in blood glucose concentration. Guar, which has the highest viscosity when mixed with water, was also found to have the most significant effect on absorption and transit time.[9] Thus, the action of guar may be twofold, depending on both delayed gastric emptying and delayed absorption of glucose in the small intestinal lumen.

In our study, there were significant reductions in both the fasting plasma glucose and the one-hour postprandial plasma glucose level following guar treatment. These findings are in general agreement with those from other clinical studies.[7,9,13] The mechanism responsible for these effects is not fully understood. Reduction in weight was not observed in our study as it was in others.[9,10,14] Increased insulin secretion is also an unlikely explanation for the effects of guar, as no change in the levels of fasting insulin and C-peptide was observed at the beginning and end of each study phase. Indeed, Fuessl et al[12] reported significant decreases in postprandial insulin and enteroglucagon responses after guar ingestion. Possible explanations for this may be improved insulin sensitivity or alteration of hepatic or peripheral glucose handling, as postulated by Jenkins et al.[20]

Another indication of better glycemic control is the highly significant drop in the HbA1 level observed during the four weeks of guar treatment. Again, this finding agrees with those reported recently and this action may well be related to delayed glucose absorption and gastric emptying.[9,21] In our study, the postprandial glucose level was considerably lower after identical test meals using placebo.

The effect of guar on the plasma lipid levels was significant. All patients with mean pretreatment values of total cholesterol of more than 6 mmol/L showed the most dramatic reduction; the level in some decreased to within our laboratory normal reference range (3.6–6.2 mmol/L) (Figure 1C). However, there was no significant change in the plasma triglyceride level, as was found in other studies.[8,12,13,15] Moreover, recent reports have also demonstrated a reduction in the ratio of cholesterol to HDL-cholesterol; by preferential effect the guar reduced the total cholesterol but not the HDL-cholesterol level.[10,14] This would be beneficial in diabetic patients who are prone to suffer from coronary atherosclerosis, since a higher HDL:LDL ratio is believed to protect against coronary artery disease in men.[22]

The predominant complaint of patients while on guar was soft stool, with or without frank diarrhea and flatulence, mostly present together in the same patient. Only three patients found guar inconvenient to take. Of the 33 patients with guar-induced side-effects, treatment was discontinued in only seven. In the remaining patients, the side-effects were mild, well tolerated, and abated with time. A high incidence of side-effects was also reported with placebo (beef gelatin), with symptoms similar to those seen with guar (mainly abdominal, i.e., soft stool, flatulence, and cramps). Only three patients were dropped from the study while on placebo because of intolerance. Since the side-effects decrease with continued treatment, perhaps the dose of guar should be lower initially and increased slowly over time to allow the patient to adjust to its effects.

In this study of a non-Caucasoid diabetic population, we have demonstrated that the effect of guar gum is equal to that observed in studies of other ethnic groups. We therefore recommend the use of guar gum as an adjunct in the management of patients with uncontrolled NIDD on maximized conventional therapy, before switching the patient to insulin therapy.

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PENETRATING ABDOMINAL INJURY: TOWARD MORE CONSERVATIVE MANAGEMENT

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أدخل مائة وتسع وثلاثون مريضا على مدار خمس سنوات إلى أجنحة الجراحة العامة في مستشفى الرياض المركزي بسبب جروح نافذة في البطن. تعرض ٥٦٪ منهم لجروح طعنية بينما كان الباقون (٤٤٪) ضحايا إصابات نارية أو بنادق الهواء المضغوط. أدخل جميع المرضى في بادي الأمر للتقييم السريري والملاحظة المعززة ببعض الفحوص المخبرية والشعاعية. اجري فتح البطن الاستقصائي على ٨٢٪ منهم. كان معدل النتائج السلبية اثناء فتح البطن مرتفعا بشكل غير مقبول إذا بلغ ٢٨٪. وقعت الوفاة والمراضة بين المرضى الذين أخضعوا لفتح البطن فقط. تؤيد النتائج المستقاة من تحليل البيانات تبني طريقة أكثر تحفظا في معالجة المصابين بمثل هذه الحالات، شريطة أن تقوّم حالاتهم بعناية وأن تتم مراقبتهم من قبل أطباء ذوي خبرة.

Over a period of five years, 139 patients were admitted to general surgical wards at the Riyadh Central Hospital because of penetrating wounds to the abdomen. Of these, 56% of the patients sustained stab wounds and the remaining 44% were victims of gunshot or compressed air gun injuries. All patients were admitted initially for clinical evaluation and observation with the aid of a few diagnostic laboratory and radiology tests. Exploratory laparotomy was performed in 82% of the patients. The rate of negative findings at laparotomy was unacceptably high at 25%. Mortality and morbidity occurred only in the patients who underwent laparotomy. Results of analysis of the data support adoption of a more conservative approach in the treatment of such patients, provided they are evaluated carefully and observed by experienced staff.

The management of penetrating wounds to the abdomen is still a matter of controversy. Many surgeons still regard surgical exploration as mandatory in almost all cases.[1-3] Undoubtedly, this attitude has been dictated by military experience. Other surgeons have adopted a more selective conservative policy, and operate only on those patients who exhibit definite peritoneal penetration.[4,5] A third group of practitioners selects the management approach according to clinical, laboratory, peritoneal lavage, and radiological findings.[6-13] In this retrospective study, we evaluated our experience in the management of penetrating abdominal injuries seen at Riyadh Central Hospital over five years (July 1983 to June 1987).

Material and Methods

We reviewed the files of all patients with penetrating abdominal injuries who were admitted to the Riyadh Central Hospital during July 1983 to June 1987.

The clinical findings, resuscitative measures, and management procedures for each patient were recorded on a form that contained 33 items.

All patients were initially assessed by the casualty officer in the accident and emergency department, and then admitted to the general surgical wards for definitive treatment.

Only patients with penetrating abdominal wounds located within the area of the fifth intercostal space to the inguinal ligament anteriorly and the ninth intercostal space to the iliac crest posteriorly were included in the study.

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All such patients had an intravenous line installed and blood was drawn for full blood count, determination of urea, electrolytes, and blood glucose content, and blood grouping. When appropriate, the urine was examined for the presence of blood and glucose. If the patient was nauseated or vomiting, a nasogastric tube was inserted. Almost all patients had erect chest and abdominal x-ray studies taken.

All patients were examined by the admitting registrar for signs of peritonitis and shock. Only those patients with obvious signs of peritonitis, evisceration of omentum or viscera, or with radiological evidence of air under the diaphragm underwent exploratory laparotomy. This was usually performed within two hours of the patient's arrival at the hospital. All other patients underwent local exploration of the wound under local or general anesthesia and put on strict clinical observation.

Results

During July 1983 to June 1987, 139 patients were admitted to Riyadh Central Hospital with the diagnosis of penetrating abdominal injury. Most of the patients (86%) were male and 58% were non-Saudi nationals. The youngest victim was a 6-year-old boy and the eldest was a 55-year-old woman; mean patient age was 26 years (Table 1).

Sharp objects, mostly knives, were the source of injury in 78 patients (56%), and 51 patients were the victims of low-velocity gunshot wounds. The remaining 10 patients (7%) were injured by compressed air guns used for industrial purposes.

Based on clinical observations and minimal diagnostic findings, 114 patients (82%) underwent exploratory laparotomy. The clinical criteria for performing laparotomy included signs of shock, abdominal wall rigidity, evisceration of intraabdominal contents, and absence of bowel sounds. Erect abdominal and chest x-ray studies along with local exploration of the wounds and peritoneal lavage were done for diagnostic purposes. In this group peritoneal lavage was done in only seven patients. Results were positive in four and equivocal in the remaining three. Local wound exploration was carried out in six patients in this group, and all underwent laparotomy afterward because findings from exploration were considered positive (deep wound, presence of viscera in the bottom of wound, and/or continuation of bleeding from the wound).

TABLE 1. *Age/nationality distribution.*

Age range (yr)	No. of victims	% of Saudis
0 - 10	13	31
11 - 20	20	30
21 - 30	79	29
31 - 40	13	62
41 - 50	8	62
51 - 60	6	33
Total	139	42

TABLE 2. *Laparotomy results in 11 patients.*

Type of penetrating injury	No. of patients	Negative laparotomy rate (%)
Stab injury	58	16 (28%)
Gunshot injury	46	2 (4%)
Compressed air gun injury	10	10 (100%)
Total	114	28 (25%)

The rate of negative findings at laparotomy was 25% (Table 2). Of the remaining 25 patients (18%; 20 stab and five gunshot injuries), none required laparotomy based on clinical findings and the findings from local wound explorations. These patients were observed closely and their clinical condition stabilized within 2 to 4 days, allowing discharge from the hospital without the need for exploratory laparotomy.

The overall mortality rate in this series was 10%, and all deaths occurred in those patients who underwent laparotomy. Two patients died on the operating table before laparotomy incision was completed; the remaining 12 patients died postoperatively. Of the remaining 96 patients, the most frequently injured intraabdominal organs found at laparotomy were the liver followed by the stomach and the diaphragm. The abdominal aorta was the least frequently affected structure (Table 3). The knife wound in one patient traversed the epigastrium, stomach, diaphragm, and inferior surface of the heart.

Discussion

Although the pattern of penetrating abdominal injuries in our series is similar to that reported in

TABLE 3. *Frequency of involvement of intraabdominal organs in 96 penetrating abdominal injuries.*

Organ affected	No. of patients	Percentage
Liver/biliary tract	38	40
Stomach	22	23
Diaphragm	22	23
Small bowel/mesentery	21	22
Large bowel/mesocolon	15	16
Spleen	9	9
Pancreas/duodenum	6	6
Kidney	5	5
Urinary bladder	4	4
Abdominal aorta/ inferior vena cava	2	2
Heart	1	1

Western series, none of our patients was drunk or under the influence of drugs.[9-16] Most of the penetrating abdominal injuries in the present series were due to direct trauma produced by sharp objects. A few of the injuries were the result of road traffic accidents and were associated with other skeletal injuries. Laparotomy was performed in almost all of this small group of road traffic accident victims. Neither the site of abdominal penetration nor the type of injury could predict the number, type, and magnitude of the injury to the intraabdominal organs.

Our policy is to admit all patients with penetrating abdominal injuries regardless of their clinical status or the appearance of the entry wound. All such patients are evaluated by the admitting registrar. The decision to explore the abdomen is almost always based on the clinical findings and few diagnostic laboratory and radiological tests. Only 18% of our patients did not undergo laparotomy and diagnosis was 100% accurate in these patients. Conversely, in the laparotomy group the rate of negative findings was high (25%). Analysis of the clinical, laboratory, radiological, and operative findings in the laparotomized group revealed that our negative rate could have been improved and we could have at least avoided laparotomy in 64% of the patients. We should have used a more conservative approach and waited more time to evaluate our patients. We should also have made more use of peritoneal lavage and stabograms, and performed more extensive local explorations of the wounds. A conservative approach does not imply withholding surgical intervention when required nor rule out the need for more diagnostic investigations. The philosophy of selective conservatism requires experience and careful interpretation of the clinical findings. We have found that the presence of shock and generalized abdominal tenderness or guarding are more reliable indicators for laparotomy. Localized tenderness or guarding and the presence of air under the diaphragm alone are much less reliable signs, especially in compressed air gun injuries that usually do not involve injury to intraabdominal organs. Nevertheless, we believe that abdominal gunshot wounds almost always require laparotomy. Some surgeons advocate the use of stabograms or sinograms to demonstrate the extent of the injury and the involvement of intraabdominal organs.[17-20] We did not use these and therefore cannot comment on their reliability. Although we use peritoneal lavage in all patients with blunt abdominal trauma, our experience with lavage for penetrating abdominal injuries is very limited and we used it in only seven patients. It is therefore difficult to draw conclusions about the merits of lavage, though literature review shows that local wound exploration coupled with open peritoneal tap and/or quantitative diagnostic peritoneal lavage are safe and cost-effective techniques for evaluating patients with anterior abdominal penetrating wounds.[11-13] The reported accuracy rate of these techniques is approximately 97%.

Our morbidity rate of 10% is comparable to those reported by others, especially proponents of mandatory surgery for all cases of penetrating abdominal injury. All our 14 deaths occurred in those patients who underwent laparotomy. The mean hospital stay of these patients was 13 days, compared with 3 days in those patients who did not have laparotomy.

All patients with penetrating abdominal wounds should be admitted to the hospital for observation, but only those who show obvious signs of hypovolemic shock, peritonitis, or evisceration of omentum or viscera should undergo laparotomy. The remaining victims who possess subtle signs should be more carefully assessed clinically and their wounds explored locally under local or general anesthesia. If this reveals penetration of the anterior peritoneum at the bottom of the wound or there is continuous bleeding through the wound or presence of feces, bile, or food material, the patient should undergo exploratory laparotomy. Those victims whose local wound exploration is negative should be carefully observed by experienced medical and nursing staff.

If unfavorable clinical signs arise, the patient should have diagnostic peritoneal lavage to determine whether he or she should have exploratory laparotomy.

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WEBBED PENIS IN ARAB CHILDREN

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القضيب الأوتر شذوذ خلقي نادر. وقد ورد في الكتابات الطبية حوالي أربعين حالة، واحدة منها لدى طفل مصري. وتضم هذه الدراسة خمس حالات أخرى، حالتين في ليبيا وثلاث حالات لدى رضع في المملكة العربية السعودية، شخصت جميعها بعد الولادة بقليل. تم خلال العملية تحرير جسم القضيب وتغطيته بالجلد واستحداث موصل قضيبي صفني. كما تم استئصال شريط ليفي وجد في حالتين. وتعرض هذه الدراسة مراجعة للأبحاث الطبية مع بعض التوصيات حول مخطط للتصنيف.

Webbed penis is a rare congenital anomaly. Approximately forty cases have been reported, one in an Egyptian baby. We report five more cases, two in Libyan and three in Saudi infants, all diagnosed soon after birth. At operation the penile shaft was released and covered with skin with recreation of the penoscrotal junction. A fibrous band, found in two cases, was excised. The literature is reviewed and some recommendations made for a classification scheme.

Webbed or buried penis, in which the penile shaft is partially or completely buried in a scrotal envelope, is a rare congenital anomaly. Since Bissotti[1] described a case in 1953 in a 13-year-old, 38 cases have been reported. Of these, one had associated syndactyly,[2] one hypospadias,[3] and three epispadias.[4] The deformity is described briefly in textbooks.[5-7] In 1977, Crawford[4] suggested a nomenclature to differentiate between the different types. Maizels et al[8] suggested another classification; however, the cases he describes do not appear to be instances of true buried penises but were buried due to localized adiposity, while one was micropenis and one diminutive penis with epispadias. Most of the cases were seen when the patients were young children, except the two earliest which were in adults.

Case Reports

Patient 1

Examination in a week-old baby revealed the prepuce of the penis from the scrotum with two areas of skin whirling. The penile shaft could be felt throughout. Three months later the patient underwent surgical repair. Following a dorsal split, a Z-plasty incision was planned to allow placement of the transverse scar at the penoscrotal junction. There was no chordee, but there was a lax whitish, fibrous band starting at the coronal level that disappeared into the scrotal subcutaneous tissue. This proved to be a fibrous band, not the chordae, and was excised. The penis was then covered with available skin in a zigzag manner, followed by circumcision.

Patient 2

The penile shaft of a 3-month-old baby, who was originally brought for circumcision, was found to be buried and the prepuce covered. The glans penis was normal, and the penile shaft could be palpated throughout. Operation incorporated a Z-plasty incision to allow formation of the penoscrotal junction. The penile shaft was normal and no fibrous band was found. Closure was

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effected in a zigzag manner and circumcision done.

Patient 3

A 3-week-old baby who was brought for circumcision was noted to have a partially buried penis. The prepuce and glans were free but the penis was found to be webbed when the shaft, which was palpable, was lifted. Through an approach similar to the one used in Patients 1 and 2, the penis was explored. At operation, a loose white fibrous band was found to be attached near the corona which disappeared into the scrotal subcutaneous tissue. This was excised. The penis was then clothed with available skin.

Patient 4

A 5-week-old infant was referred to our outpatient clinic for circumcision, as the scrotal skin was attached to the ventral penal skin. Webbed penis was evident on examination. The infant underwent surgical repair similar to that undergone by Patient 3; however, no fibrous band could be found. Circumcision was done at the same time.

Patient 5

A 6-week-old infant came for circumcision and at that time was found to have a webbed penis (Figure 1). This patient's case was similar to that of Patient 4.

All patients were followed in our outpatient clinic for 2 to 4 years and during that time showed normal development. No chordee was found on stimulation of the glans penis.

Discussion

Circumcision is widely practiced in the Middle East, mainly for religious purposes. It is performed soon after birth[9] in spite of the position of the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists that "there is no medical indication for routine circumcision."[10] There is evidence that this procedure reduces the incidence of urinary tract infection, as shown by the studies of Wiswell et al.[11-13] They also showed an eleven-fold increased incidence of urinary tract infection in uncircumcised boys, compared with circumcised boys.[12]

It has also been reported that there is a higher incidence of human immunodeficiency virus infection in uncircumcised African boys, suggesting that the intact skin increases the susceptibility to this infection.[14]

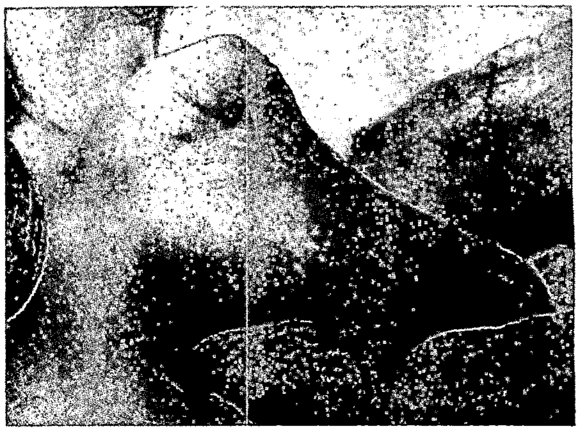

FIGURE 1. Buried penis with prepuce emerging from the scrotum.

Normally the penis is clothed in hairless skin that merges with scrotal skin at the penoscrotal junction ventrally and with abdominal skin dorsally. The defect occurs when there is a deficiency of skin. The penis becomes buried in scrotal skin if the ventral skin is deficient and in the suprapubic abdominal skin if the dorsal skin is deficient. Review of the reported cases revealed that several categories have been grouped together (Table 1). Crawford[4] suggested a nomenclature with which we agree, except that we feel another type should be added to reflect a basic difference that exists in the siting of the skin deficiency. Maizels et al[8] formulated a classification as well, but according to their scheme, our cases would be considered concealed penis, which is not an accurate description. We therefore propose the following classification.

Group I: Concealed Penis

In this category, the penis is normally clothed and the skin is present. Either the organ is concealed by excess surrounding subcutaneous fat, or the skin is lifted off the penis by large bilateral hydroceles.

Group II: Webbed Penis

Here the normal penis is fully clothed with skin but there is a web of skin extending from the area of the penile raphe. The web may start just behind the prepuce or more proximally. The defect in this group may be associated with hypospadias.

TABLE 1. *Summary of cases of webbed penis reported in the literature.*

Author	Year	No.	Ages	Associated anomalies	Treatment	Comments
Bissotti[1]	1953	1	13 yr	None	N/A	--
Glanz[2]	1968	1	57 yr	Syndactyly	N/A	Completely buried penis
Perlmutter et al[15]	1972	6	6 mo to 12 yr	None	Linear closure or Z-plasties	1 case report only, webbed penis with adequate skin
Kinawi[16]	1973	1	5 yr	None	Excision of inverted T closure	Webbed penis with adequate skin
Masih et al[3]	1974	3	2½ yr to 10 yr	Hypospadias in one case	W-plasties	Skin adequate in 1 & 2, the third patient had hypospadias
Puri[17]	1976	1	3½ yr	None	V-shaped incision	--
Crawford[4]	1977	6	N/A	Epispadias in 2 cases	S-shaped incision dorsally and use of prepuce	No individual case report; main emphasis on dorsal skin shortening. Need for grafting of dorsum
Shephard[18]	1980	1	1 yr	None	W-plasties with rectangular flap ventrally	Abundance of skin
Redman[19]	1985	8	5 mo to 5 yr	1 hypospadias, 1 torsion penis	--	--
Azmi[20]	1986	3	3–4 yr	None	Transverse incision, vertical closure	Redundancy of skin
Maizel et al[8]	1986	7	2 mo to 14 yr	Epispadias in one case	Excision of adipose tissue	5 concealed penis, 1 micropenis, 1 diminutive penis with epispadias
Present series	1990	5	3 wk to 4 mo	None	Z-plasty for penoscrotal and zigzag closure	Adequacy of skin in 4 cases

N/A = not available.

Group III:

(A) This subclassification consists of buried penis, with ventral skin deficiency. Here the penile shaft is normal but is deficient and is partially or completely buried in the scrotal envelope, except for the prepuce which is present.

(B) This subgroup constitutes those cases with buried penis that are affected by dorsal skin deficiency. Here the penis is buried in the suprapubic abdominal skin. There may be associated epispadias.

We consider micropenis a completely different anomaly, as the defect has to do with penile shaft development, not penile skin deficiency and with a normally formed penis. From a developmental perspective, most authors think that this defect is due to disturbed development of the prepucial skin.[3,15] However, this is contradicted by the finding that the prepuce is well formed in all reported cases. We agree with Kenawi[16] that there is probably failure of migration of the penoscrotal fold posteriorly.

Treatment

Group I patients do not need any operation on the penis, but operation on the hydrocele, or removal or reduction of excess fat to unveil the organ.

Group II and III-A patients require creation of a penoscrotal crease and clothing of the shaft. In all reported cases, sufficient skin was available to allow performance of a Z-plasty so that the penoscrotal junction could be formed, with zigzag closure on the ventral aspect to avoid a linear scar. Prepucial skin and mucosa may be borrowed when necessary and excess excised or left depending on whether circumcision is to be done. Innes-Williams[21] has cautioned against early operation, since this may interfere with penile growth. Our feeling is that early operation does not carry this risk, though admittedly in our patients follow-up is short. We think that operation is best done when convenient, preferably around three months of age but definitely before school age.

Group III-B patients require a dorsal S-shaped incision, as advised by Crawford,[4] with excision of the fibrous band, if present, that tethers the penis to the pubis. The exposed area on the dorsum of the penis should then be covered with flaps from the redundant ventral prepucial skin. Occasionally this may not be sufficient and the residual area may need a split skin graft. Epispadias, when present, may be corrected later.

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RADIOGRAPHIC PROFILE OF SPONDYLOLYSIS AND SPONDYLOLISTHESIS IN SAUDIS

Tajuddin Malabarey, FRCR; Dorothy Makanjuola, FRCR

جرى تحليل ١٥٥٤ حالة متعاقبة لمرضى احتاجوا إلى تقييم شعاعي للفقرات القطنية العجزية لاستقصاء سبب ألم في أسفل الظهر متفاوت المدة فظهر أن ١٧١ مريضا (١١٪) منهم يعانون من انزلاق الفقار. كان أكثر الأنماط تواردا انحلال الفقار (٦١٪) تلاه النمط الثدني (٢٣٪) فالتنكسي (١٤٪). وقع انحلال الفقار مع انزلاق الفقار أو بدونه لدى ١٣٦ مريضا (أي ٩٪ من المرضى الذين أجري لهم التصوير الشعاعي بسبب ألم أسفل الظهر). تأثر المرضى من جميع الأعمار بالنمطين الثدني والانحلالي معا مع ذروة انتشار بين سن العشرين والأربعين. واقتصر النمط التنكسي عموما على النساء فوق سن الأربعين. لم يمكن إظهار أية عوامل مؤهبة متميزة كالتمارين أو المهنة أو تاريخ الأسرة. إلا أن نمط الحياة القعودي، في النوع التنكسي، الذي ينطوي على الجلوس لفترات طويلة يمكن أن يكون عاملا مسببا لألم أسفل الظهر. إن اكتشاف الإصابة بانزلاق الفقار لا يلزم بالقول بمسؤوليته السببية. ولابد من إجراء المزيد من التقييم المفصل بتصوير القناة الفقرية الظليل والتصوير الطبقي بالكمبيوتر والتصوير بالطنين المغناطيسي في الحالات التي يكون فيها الألم شديدا.

An analysis of 1554 consecutive cases of patients requiring radiographic evaluation of the lumbosacral spine to diagnose the cause of low back pain of varying duration shows that 171 patients (11%) had spondylolisthesis. The three major types consisted of: dysplastic (congenital), isthmic (spondylolytic), and degenerative. The most common was spondylolytic (61%), followed by the dysplastic (23%), and then degenerative (14%). Spondylolysis, with or without spondylolisthesis, occurred in 136 patients (i.e., 9% of patients who underwent radiography for low back pain). Patients of all ages were affected by both the dysplastic and spondylolytic type, with a peak incidence between 20 and 40 years of age. The degenerative variety is largely a disease of women over 40 years of age. No distinct predisposing factors, such as exercise, occupation, or family history, were elicited. However, in the degenerative variety, a sedentary lifestyle involving prolonged sitting could be a causative factor. The discovery of spondylolisthesis does not necessarily incriminate the cause. More detailed evaluation with myelography and computed tomographic or magnetic resonance imaging is mandatory in cases in which there is unrelenting pain.

Spondylolisthesis is the forward slipping of one vertebra onto another, or the forward slipping of the whole lumbar spine in relation to the sacrum. It was first recognized by the Belgian obstetrician Herbiniaux[1] in 1782 and was subsequently named "spondylolithesis" by Killian[2] the following year. Spondylolysis implies a defect in the pars interarticularis of the neural arch and was first described by Roberts in 1855.[3]

In the past, all cases of spondylolisthesis were considered the result of spondylolysis and the neural arch defect was considered congenital in origin. It is now clear that spondylolysis is only one of the causes of spondylolisthesis and that not all cases of spondylolysis are congenital in origin.

Spondylolisthesis is now classified into five major groups, as suggested by Wiltse.[4] These are dysplastic, isthmic or spondylolytic, degenerative, traumatic, and pathological spondylolisthesis. The dysplastic variety is congenital in origin. It

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occurs at the lumbosacral junction and involves slipping of the last vertebra onto the sacrum. Developmental anomalies such as sacral spina bifida and deficiency of the superior sacral facet are also usually present. There is also attenuation of the lamina of the last lumbar spine. The isthmic or spondylolytic type is due to a defect in the pars interarticularis of the neural arch and constitutes the well-known spondylolysis. Degenerative spondylolisthesis is due to osteoarthritis of the posterior facet joint, while traumatic spondylolisthesis is the consequence of severe spinal injury causing fracture displacement of the vertebral body. The pathological variety is due to tumor or inflammation affecting the bone.

The etiology of spondylolisthesis has been ascribed to various factors, including a congenital origin with a high family incidence reported by various authors.[5-7] There is also mounting evidence implicating minor trauma such as exercise and repetitive activities.[8-10] Racial and sex variations have also been observed with a high frequency of 45% seen among certain Eskimo groups[7] and a low frequency of 1.1% among black females compared with a 6.4% frequency among Caucasian males.[11]

The present study is the first one, to our knowledge, to examine the pattern and possible causes of the disorder as observed in this part of the world. This investigation was stimulated by the apparent frequency with which we encountered spondylolysis and spondylolisthesis in radiographs of the lumbar spine obtained in patients being evaluated for low back pain at King Khalid University Teaching Hospital, Riyadh.

Material and Methods

A prospective study of 1554 consecutive lumbar spine x-ray studies done over a period of six months was undertaken. Initially anteroposterior and lateral projections were obtained. Oblique views were obtained when the conventional ones were ambiguous. Patients with spondylolisthesis were classified according to the five major groups defined by Wiltse,[4] i.e., dysplastic, spondylolytic, degenerative, traumatic, and pathological. The degree of displacement was graded on the basis of I to IV according to the fractional shift of the vertebras observed on the lateral projection, and according to the grading schemes of Meyending.[12] In Grade I, less than one fourth of the vertebral body is displaced. Grade II involves displacement of about half the vertebral body. Grade III involves displacement of three fourths of the vertebra, while Grade IV involves displacement of more than three fourths of the vertebral body. Associated vertebral anomalies were also noted for patients in the series. Cases of spondylolysis without spondylolisthesis were also recorded.

TABLE 1. *Distribution of the type of spondylolisthesis affecting 171 patients.*

Group	No. of cases	Percentage	Males	Females	Male to female approx. ratio
Dysplastic	39	23	23	16	3:2
Spondylolitic	104	61	68	36	2:1*
Degenerative	24	14	5	19	1:4*
Pathological	4	2	2	2	1:1
Total	171	100	98	73	--

* Statistically significant at $P < 0.01$.

TABLE 2. *Age incidence of the three most common types of spondylolisthesis in the 156 cases with recorded age.*

Age (yr)	Congenital	Spondylolisthesis	Degenerative
0 - 10	1	1	0
11 - 20	2	5	0
21 - 30	8	30	0
31 - 40	10	26	0
41 - 50	5	14	2
51 - 60	5	10	12
61 - 70	3	9	5
Over 70	2	4	2
Total	36	99	21

The following information was also obtained. Nationality, age, sex, occupation, hobby, family history of the disorder, recent or old trauma, and the presence or absence of symptoms.

A chi-square test was used to investigate the association between sex and the various types of spondylolisthesis. This is declared significant at the 5% level.

Results

Table 1 shows the distribution of the types of spondylolisthesis encountered and the sex distribution. Of the 1554 consecutive cases studied, 171

(11%) had spondylolisthesis. Figure 1 illustrates the common types of spondylolisthesis encountered. Table 2 shows the breakdown according to age of the three common types of spondylolisthesis for the 156 patients for whom age was recorded.

The spondylolytic type constituted the largest variety (61%), followed by the dysplastic (23%) and then degenerative type (2%). The traumatic type was not encountered, probably because the hospital is not primarily a trauma treatment hospital.

A significant male preponderance was found for the spondylolytic variety ($P < 0.01$) while the degenerative types showed a significant female preponderance ($P < 0.01$). Although a male preponderance was found in the dysplastic variety, this sex differential was not statistically significant (Table 1).

Both the spondylolytic and dysplastic variety showed a peak frequency between the second and fourth decade. The degenerative variety was not observed in patients before age 40, and the peak frequency was between the fifth and sixth decades.

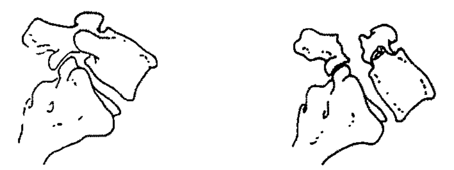
Vertebral displacement was seen largely in cases of Grade I or II spondylolisthesis and occurred in 158 (92%) of the cases. Thirty-two patients had spondylolysis without spondylolisthesis and these cases were mainly unilateral.

The L-5 vertebra was involved in 106 cases (62%) followed by L-4 in 59 cases (34%). The remaining cases were distributed between L-3 and L-4. In two cases, multiple levels were involved with no history of trauma. Involvement of L-5 was commonly associated with the spondylolytic and degenerative types.

The main clinical presentation was low back pain, and a history of trauma was rare. No notable pattern of family or occupational history was seen. Analysis of the breakdown according to nationality showed that 149 of the 171 (87%) were Saudis, 10 (6%) were Yemeni, and the remaining 12 (7%) were of various other nationalities.

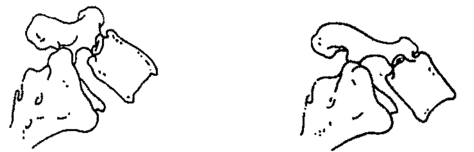
Discussion

Our study reveals an 11% incidence of radiographically detected spondylolisthesis in patients being investigated for back pain. This is more than the 5% incidence reported by Wiltse[13] for adult populations of the United States, but similar to Banna's[14] finding of 10% among patients with back pain who seek the aid of a physician.



Normal

Spondylolytic Spondylolisthesis



Degenerative Spondylolisthesis

Dysplastic Spondylolisthesis

FIGURE 1. The normal spine and the common types of spondylolisthesis.

The main clinical presentation for the patients in our series was low back pain of varying duration. No significant pattern of family or occupational history was observed nor were the types of hobbies or sports engaged in by the patients of significance. A past or present history of trauma was also uncommon.

The most common type of spondylolisthesis was spondylolytic (Figure 2), which was seen in approximately 7% (104 of 1554) of the cases of low back pain presenting for radiographic evaluation. However, a pars interarticularis defect without displacement occurred in 32 cases, most of which were unilateral. The primary feature was a fracture which varied from a hairline crack to a distinct separation of 5 mm or more. Degenerative changes frequently commenced following spondylolisthesis, and in its advanced form could mimic an infective process with resorption of the articular surfaces of the vertebra (Figure 3). This commonly occurred at L-4/L-5, which is presumably the most mobile lumbar level.

The dysplastic type (Figure 4) was the second most frequently encountered form of spondylolisthesis. The main features, as described by Newman,[15] consisted of involvement of the lumbosacral junction with slipping of the last lumbar vertebra onto the sacrum, the presence of developmental anomalies such as sacral spina bifida, and deficiency of the superior sacral facet or inferior process of the L-5 vertebra, which is often attenuated. There is usually no break in the pars interarticularis, as occurs in the spondylolytic type.

All age groups were affected, with a peak incidence between the second and fourth decade.

Degenerative spondylolisthesis was third in frequency. There was a distinct female preponderance, with a female-to-male ratio of 4:1. The peak incidence was in the fifth and sixth decades and no cases were in patients younger than 40 years of age. These findings are similar to those reported in other studies.[14,15] The basic abnormality is osteoarthritis of the zygapophyseal joint, which

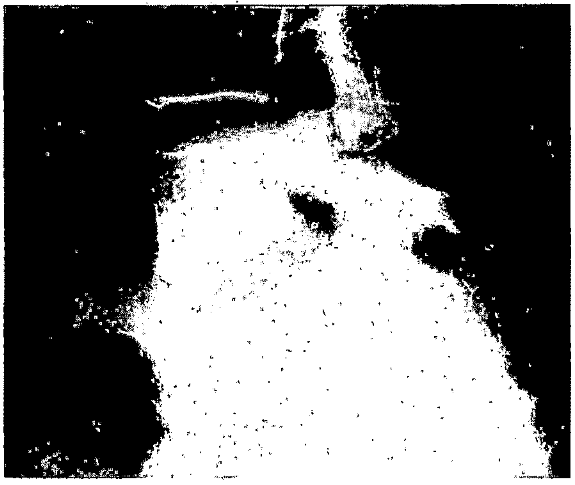


FIGURE 2. Lateral view of the lumbosacral junction showing Grade I spondylolytic spondylolisthesis. Note elongation of the pars interarticularis of L-5 as well as a fracture in the area.

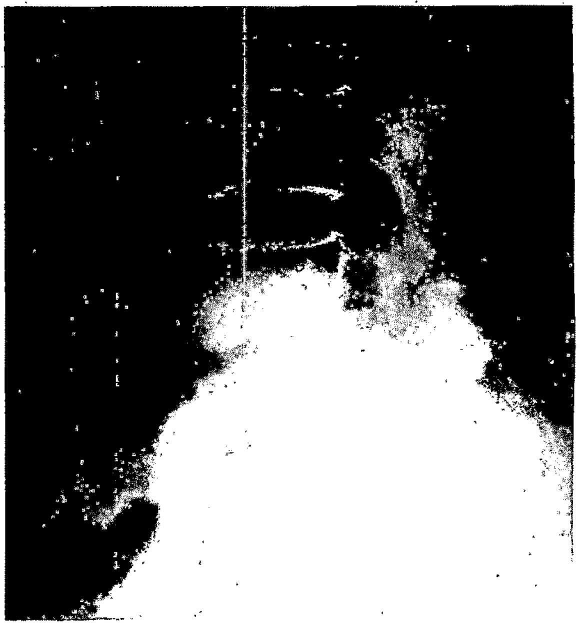


FIGURE 3. Lateral view of the lumbosacral spine showing Grade II spondylolytic spondylolisthesis with advanced degenerative changes of L-4/L-5 simulating an infective process. There was no clinical or laboratory evidence of infection at this level.

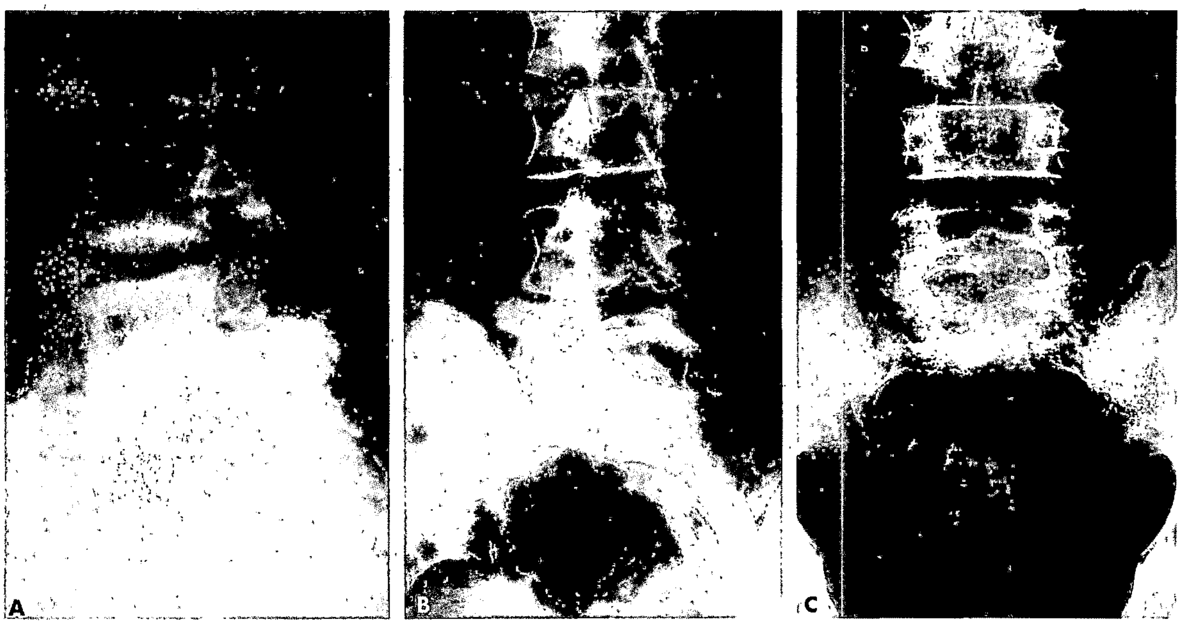


FIGURE 4. (A) Lateral view of the lumbosacral junction showing Grade I dysplastic spondylolisthesis with both anterior and posterior elements of L-5 sliding forward. (B) Oblique projection showing deformity of the inferior articular facet of L-5 as well as elongation and thinning of the lamina. (C) Anteroposterior projection revealing the usual associated sacral spina bifida and thinned lamina.

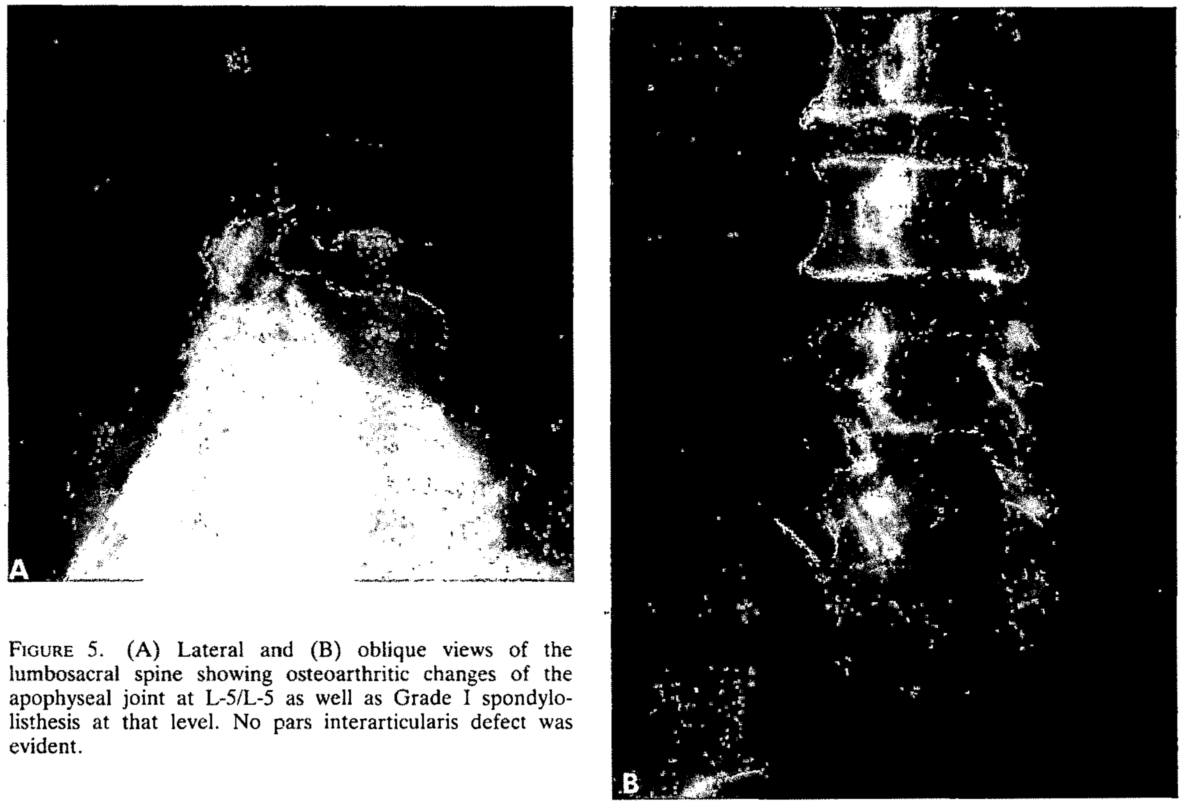


FIGURE 5. (A) Lateral and (B) oblique views of the lumbosacral spine showing osteoarthritic changes of the apophyseal joint at L-5/L-5 as well as Grade I spondylolisthesis at that level. No pars interarticularis defect was evident.

renders the joint inadequate. There is forward displacement of a lower lumbar vertebra, commonly at L-4 (Figure 5). The neural arch is usually intact.

The sex and age distribution raises the possibility that a sedentary lifestyle that involves prolonged sitting could well be a predisposing factor.

The pathological form of spondylolisthesis was the least common. Four cases were found, yielding an incidence of 2%. Two cases were due to metastatic deposits, while the other two were the result of an infective process, either previous tuberculosis or brucellosis. The discovery of spondylolisthesis in a patient with low back pain does not necessarily indicate that the vertebral displacement is the cause of the pain. However, in patients with unrelenting pain, myelography with computed tomographic evaluation or magnetic resonance imaging, if available, is prudent.

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EPIDEMIOLOGY AND PARENTAL PERCEPTION OF NOCTURNAL ENURESIS IN ARAB SCHOOLCHILDREN

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أجريت دراسة مقطعية، وصفية وضابطة على عينة عشوائية شملت ١٢٦١ من تلاميذ المدارس الابتدائية تراوحت أعمارهم من ٦ إلى ١٠ سنوات، وذلك بهدف تقييم انتشار مشكلة بول الفراش ومدى ارتباطها بالعوامل النفسية والنمائية والعضوية والاجتماعية - الاقتصادية. استخدمت لهذا الغرض استبيانات ذاتية التطبيق وتم استرجاع ١٠٤١ منها. بلغت نسبة انتشار بول الفراش ٩٧ في الألف وبلغت فيها نسبة الذكور إلى الاناث ١,٣:١ وكان هناك ترابط احصائي هام بين مشكلة بول الفراش والاكثار من شرب السوائل قبل النوم، ونمط النوم العميق، والتأخر في النطق، والتوتر النفسي، اعتبر أهالي الأطفال الذين يعانون من مشكلة بول الفراش أن الحدّ من شرب السوائل قبل الذهاب إلى النوم هو أفضل وسيلة لمنع حدوثها، في حين اعتبر أهالي الأطفال الذين لا يعانون من هذه المشكلة أن التبول قبل النوم يأتي أولا. كما أن ١٤٪ فقط من أهالي الطلاب الذين يبولون في الفراش طلبوا مساعدة الطبيب النفسي لعلاج أطفالهم. بينما لم يعرب سوى ٣٪ فقط من أهالي الأطفال الذين لا يعانون من هذه المشكلة أنهم كانوا سيطلبون مثل هذه المساعدة لو كان أطفالهم يعانون منها. إن نسبة انتشار مشكلة بول الفراش في المجتمع يجب أن تنال الاهتمام الجدي الذي تستحقه من جانب المسؤولين التربويين والصحيين.

In a cross-sectional, descriptive, and case control study, a sample of 1261 primary schoolchildren, aged 6 to 10 years, was randomly chosen for the purpose of assessing the prevalence of nocturnal enuresis (NE) and its correlation with psychological, developmental, organic, and socioeconomic factors. Self-administered questionnaires were used, and 1041 of the forms were retrieved. The prevalence of NE was 97 per 1000 schoolchildren, with a male to female ratio of 1:1.3. There was a statistically significant correlation between NE and excessive drinking before retiring to bed, a deep sleep pattern, delay in speech acquisition, and tension habits. Restriction of fluid intake before retiring to bed was considered the best method to avoid bedwetting by parents of enuretics. Parents of nonenuretics ranked urination before going to bed first. Only 14% of the bedwetters' parents had sought medical or psychiatric help for their child and only 3% of the nonenuretics' parents indicated they would seek such assistance if their child were an enuretic. The prevalence of NE in the community merits the serious attention of both educational and health care delivery personnel.

Nocturnal enuresis (NE) is a common and bothersome problem for children as well as their parents. When defined as bedwetting that occurs at least once a month, its prevalence in the Western countries is between 13 and 21% among 5-year-old children.[1,2] If defined in terms of occurring at least once a week, the prevalence is between 6 and 7%.[1,3] Being a symptom and not a disease, its origin is multifactorial. Genetic factors, bladder function, psychological stress, psychiatric illness, and depth of sleep are some etiological mechanisms to be considered, along with organic causes like urinary tract infections and abnormalities.[4] Little is known regarding the attitudes

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of parents toward the problem of bedwetting in their children, even though it may adversely affect the parent-child relationship. Information regarding the parental perception of NE may guide physicians in better dealing with the problem.

The aim of this study was to describe some aspects of the epidemiology of NE in an unselected population of Arab schoolchildren. In addition to the prevalence and sex distribution, we have analyzed the importance of psychological and behavioral factors, the relationship between NE and developmental delay, and the occurrence of NE as related to delayed toilet training. The significance of a positive family history and the association between NE and socioeconomic factors is examined, including a detailed analysis of the parental perception of the problem.

Patients and Methods

A random sample of 1216 schoolchildren was drawn by stratified sampling technique from all primary schools in the five educational districts of the State of Kuwait during January and February 1987. Two primary schools, one for boys and one for girls, were chosen randomly from each district. In each school, pupils were selected randomly from four classes, primary I through IV. Self-administered questionnaires were handed out (available on request). Each pupil received a copy to be filled in by the parents and this was collected the following day. The primary school population in Kuwait totalled 124,097 students during 1968 to 1987, with an uneven distribution among the five districts; therefore the questionnaires were distributed according to these percentages, but maintaining equal distribution between the sexes. Based on the definition by Feldman[5] that NE means "the night-time wetting of two or more times per week," we regarded a control as a child who never wets the bed. Children who wet the bed less than twice a week were considered marginals and were not included in the study. From all cases received, an equal number of controls were matched according to age, sex, and grade in school.

The questionnaire consisted of 45 items dealing with socioeconomic status as well as psychological, behavioral, and developmental factors, toilet training methods, associated medical information, family history, and parental perception. Detailed questions to define parental perception included the age at which they expected a child to achieve bladder control and their methods for dealing with the problem. Parents of nonenuretic children were asked to answer as if their child were a bedwetter.

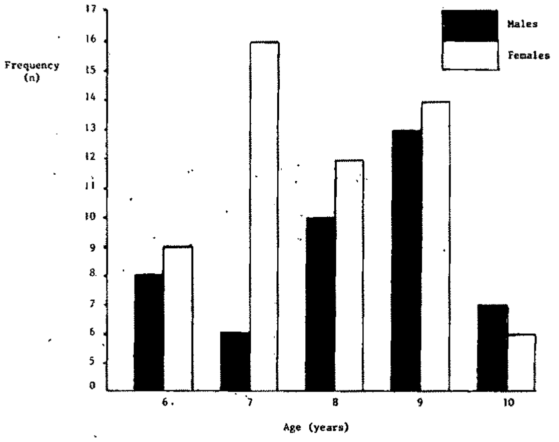

FIGURE 1. Age and sex distribution in the 101 children with nocturnal enuresis.

Standard statistical methods were applied, including chi-square and Z tests to determine differences between cases and controls.

Results

Of the 1216 questionnaires distributed, 1041 were retrieved (85.6%). The total number of children fulfilling the criteria for NE (two or more bedwetting episodes per week) was 101, yielding a prevalence of 9.7% in children aged 6 to 10 years. Thirty-nine children (3.7%) experienced NE less than twice weekly.

There were 44 boys and 57 girls in the sample of enuretic children, with a male to female ratio of 1:1.3. Girls outnumbered boys at all ages, except in the 10-year-old age group, but the difference was most marked among the 7-year-olds (Figure 1). The mean age for boys was 8.1 years and for girls 7.8 years, but this was not significant at $P = 0.2$.

Fifteen of the pupils (14.9%) with NE also had daytime enuresis. Seventeen children (16.8%) had gone for at least three months without a bedwetting episode. Among these, NE started in 11 (64.7%) at the birth of a sibling. In one child the NE started after the death of a close relative.

Sixty-six of the children with NE (65.3%) had at least one sibling with the same problem. Forty parents admitted having had NE when they were children. Fifty-four (53.5%) children had cousins who had had NE.

The psychological and behavioral factors analyzed and subsequent findings are summarized in Table 1. Factors that proved to be statistically significant were excessive drinking before bedtime, the child being a deep sleeper (as viewed by the parents), speech problems, and tension habits including nailbiting, teeth-grinding, and finger-sucking. Other factors studied did not prove to be statistically significant.

Two developmental factors were chosen that parents could easily remember. These were speech development and walking. We found a significant difference in the development of speech between affected children and controls ($P < 0.05$). Children with NE started saying single words at a mean age of 12.5 months, whereas in controls the mean age for this was 10.3 months. There was no significant difference between controls and affected children with regard to walking. The mean age (in months) when the children started walking was 12.5 and 12.6, respectively.

No statistically significant association was observed between delayed toilet training and the occurrence of NE.

In assessing the relevance of organic factors in NE, no case of diabetes mellitus or diabetes insipidus was detected in either study group. A past history or recent complaints of symptoms referred to the urinary tract, indicating urinary tract infection, were noted in 20 children with NE (19.8%) but in only six controls (5.9%; $P < 0.05$).

In assessing socioeconomic factors we found that the majority of enuretics belonged to the upper socioeconomic class (Table 2). The crowded living conditions of the families, defined as the number of children exceeding five, whether the family housed persons other than immediate family members, and whether the child had his or her own bedroom proved to be of no significance in relation to NE. When the level of education of mothers of enuretic children was compared with that of mothers of nonenuretic children, no statistical significance was seen.

Eighty-three parents of enuretic children and 95 parents of controls answered the questions regarding expected age of bladder control. The mean age expected by parents of enuretics was 7.2 ± 4.1 (SD) years and by parents of nonenuretics this was 4.2 ± 2.9 years. This difference is statistically significant at $P < 0.001$.

We asked parents about the methods they used to control the bedwetting in their children, or in those parents of control children, what methods they would employ. Eight-seven and 99 parents responded, respectively (Table 3). Restriction of fluid intake before bedtime was ranked first by 45% of the parents of the enuretics, who also considered waking up the child to urinate as the second best method (31%). Parents of nonenuretics considered urination before bedtime the best method, followed by restricted fluid intake. Waking up the child to urinate was ranked third by this group. Nine percent of the parents of enuretics considered that nothing should be done about the problem, compared to only 1% of the parents of the nonenuretics. Faith healers and traditional

TABLE 1. *The association of different psychological and behavioral factors with nocturnal enuresis.*

Factor	Cases (N = 101)	Controls (N = 101)	*P*
Marital problems	15	15	NS
Family arguments	11	6	NS
Speech problems	12	3	< 0.05
Tension habits	33	20	< 0.05
Shyness	40	45	NS
Excessive drinking before bedtime	37	10	< 0.05
Toilet before bedtime	85	88	NS
Deep sleep	41	17	< 0.05
Sleep disturbance	15	13	NS
Poor school performance	4	3	NS
School problems	22	12	NS

NS = not significant.

TABLE 2. *The association of socioeconomic status with nocturnal enuresis.*

Factor	Cases (%)	Controls (%)
Low class	6.4	11.2
Middle class	30.9	32.7
Upper class	62.7	56.1
More than 5 siblings	58.5	55.4
Has own room	15.9	18.5
Home shelters others	25.6	26.1

N.B. The total number of families responding to questions on class was 94 for cases and 98 for controls. The total number responding to questions on home living conditions was 82 and 92, respectively.

TABLE 3. *Methods tried and/or suggested by parents to achieve dryness.*

Method	Cases, N (%)	Controls, N (%)
Restrict drinking before bedtime	39 (45)	365 (36)
Wake the child to urinate	27 (31)	24 (24)
Urinate before bedtime	26 (30)	58 (59)*
Reasoning with the child	14 (16)	18 (18)
Seek professional help	12 (14)	3 (3)*
Nothing	8 (9)	1 (1)*
Faith healing and Arabic medicine	3 (3)	0
Scolding and punishment	1 (1)	5 (5)

* = $P < 0.05$.

Arabic medicine practitioners had been consulted by three parents of enuretics, whereas none of the parents of nonenuretics considered this a suitable method. Only 3% of the nonenuretics' parents indicated they would seek medical or psychiatric help if their child were a bedwetter, whereas 14% of the bedwetters' parents had sought such assistance. Scolding and punishing the child was not considered a suitable method for dealing with the bedwetting by either group of parents.

Discussion

Our study revealed some aspects concerning the epidemiology and perception of NE in Arab schoolchildren. However, studies such as ours that derive their data from self-administered questionnaires without corroborative data must be interpreted with care. Without having tested the validity of the questions for each pupil, we believe our findings are valid, based on observations from an ongoing study on treatment of enuretics. Some of our findings agree with those reported elsewhere but disagree with others.[6] We think this reflects the fact that NE is a multifactorial symptom with dispositional and situational factors that vary depending on the ethnic group studied.

The prevalence rate of 9.7% found in our study is high compared to those reported from most other studies,[1-3,7-9] but is similar to other rates cited.[5,10] It does represent, however, the actual prevalence of NE in Kuwait, as the population studied is representative for the school population of the country as a whole. Regarding the sex ratio, in most studies boys outnumber girls by a ratio of 3:2, but in our study the ratio was 1:1.3. This finding may be accidental.

We noted daytime wetting in almost 15% of our subjects with NE. When calculated from the whole sample of cases, this means that 1.4% had diurnal enuresis, which is less than the figures reported by others.[6] We did not examine these cases in detail with regard to low functional bladder capacity, detrusor instability, or bladder neck abnormalities,[11] and therefore we do not know whether these associated abnormalities were responsible for the daytime wetting, or whether the pattern was due to the same factors responsible for the NE.

Stressful events are known to be associated with the development of secondary enuresis, the likelihood of enuresis being proportional to the severity of stress. In our material, bedwetting developed in approximately one of nine enuretics following the birth of a sibling.

Many studies have focused on a positive family history of NE.[8,10,12] Our finding that 40% of enuretic children have at least one parent with a past history of NE is similar to the 43% reported by Lauver.[10] We also found that 65% of our enuretic children had at least one sibling with the same problem. Elian[13] reported 73% for this finding.

An association between a deep sleep pattern and NE has been demonstrated in several studies,[4,5,8,10] and we also found a strong association ($P < 0.01$). It has been suggested[4] that NE occurs just after the deepest sleep, when the electroencephalogram shows the arousal pattern. This stage is associated with autonomic behavior and is supposed to last longer in enuretics than others. However, related disorders, like somnambulism and sleeptalking, were not signficiantly noted in our study.

It has been stated[8] that one fourth of enuretic children have either speech problems or delayed speech development. We also noted this, but we found this in a smaller percentage, 12% versus 3% of the controls. Various types of tension habits have also been reported but discredited by others.[12,14] Our finding that 36% of children with NE also exhibit tension habits illustrates that psychogenic factors alone are important but not sufficient to precipitate NE.

We found a highly significant association between NE and excessive fluid intake before bedtime, but there was no significant association between NE and whether the child empties the bladder before bedtime. No case control study has considered this before. Some of our children may have either a small bladder capacity or an undefined[11] hypersensitive bladder.

Some investigators have reported that NE is more frequently seen in children of low socioeconomic status,[8,15] but we observed the opposite, with almost two thirds of the children coming from the upperclass. This may, like the sex ratio, be an accidental finding or may reflect a greater readiness of upper-class parents to admit to a socially less acceptable behavior in their children. We also found that neither family size nor the level of education of the mother has any bearing on enuresis. Our results contradict those obtained by others,[15] but we think this is due to lack of appropriate control groups in these respects. Our findings may also reflect the general situation in Kuwait where most families are quite well off.

In the final part of our study, we analyzed the perceived impact of NE on the enuretic child's family. The most conspicuous finding is that most parents of both enuretic and nonenuretic children did not consider NE a problem worth seeking professional help for. This contradicts the findings in an American study[16] where 48% of the parents interviewed sought help. Very few (14%) of the parents had tried reasoning with their enuretic child. A similar percentage of control parents indicated they would adopt this approach if their child were an enuretic. In the American study, 81% of the parents supported this approach. These discrepancies illustrate that parents of Arab children in Kuwait do not perceive NE as a medical or emotional disorder requiring medical or psychiatric help, but rather as a natural phenomenon that the child will eventually grow out of. This is further supported by the parental expectations concerning age at which bladder control is achieved, 7.2 and 4.2 years, respectively, for enuretic and nonenuretics in our study. In the study of American children, parents expected bladder control to be achieved by 3.2 years of age.

American parents used a combination of strategies to achieve night dryness in their children. Arab parents do not appear to do so. Some of the strategies tried, like fluid restriction before bedtime and waking up the child in the middle of the night to urinate, ranked high in both studies.

Possible explanations for the difference between Arab and Western parents concerning the perceived impact of NE might be differences in child-rearing techniques or attitudes, or it may be a question of the parent-child interaction surrounding the toilet training process.

Acknowledgments

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ACUTE HEMORRHAGIC CONJUNCTIVITIS: AN ENTEROVIRUS TYPE 70 OUTBREAK IN GIZAN, SAUDI ARABIA

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التهاب الملتحمة النزفي الحاد خمج حُموي تسببه «الحُمة المعوية ـ ٧٠» وأحيانًا «الحُمة الككساكية أ ـ ٢٤». تستعرض هذه الدراسة وباء التهاب الملتحمة النزفي الحاد في جيزان والذي يعتبر، حسب معرفتنا، أول وافدة من هذا الوباء ناجمة عن «الحُمة المعوية ـ ٧٠» تسجل في المملكة العربية السعودية. فحصنا ما مجموعه ٤١ مريضا مصابين بالتهاب الملتحمة النزلي الحاد، كان من بينهم ٢٩ ذكرا (٧١٪) و ١٢ أنثى (٢٩٪) وكان ٢١ مريضًا (٥١٪) دون سن العشرين. هجم المرض بصورة مفاجئة وبلغ ذروته خلال ساعات قليلة. وكانت أبرز خصائصه النزف تحت الملتحمة (٣٢ مريضا، ٧٨٪) وضخامة العقد اللمفية أمام الأذنيين (٣٠ مرضا، ٧٣٪). عزلت «الحُمة المعوية ـ ٧٠» من أربعة سحاجات ملتحمية من أصل ٢١. وكان السبب في نجاح العزل هو الحصول على هذه السحاجات في المراحل الأولى للمرض (خلال ٤٨ ساعة) وإرسالها إلى المختبر على الفور (خلال ٣ ساعات).

Acute hemorrhagic conjunctivitis (AHC) is a viral infection caused by enterovirus type 70 but can occasionally be caused by coxsackie virus type A-24. We report an epidemic of AHC in Gizan which, to our knowledge, is the first known outbreak of AHC caused by enterovirus type 70 witnessed in the Kingdom of Saudi Arabia. We examined a total of 41 patients with AHC. Twenty-nine (71%) patients were male and 12 (29%) were female. Twenty-one (51%) were under the age of 20 years. Onset in all patients was abrupt and the disease peaked within a few hours. The most common characteristics of the illness were subconjunctival hemorrhage (32 patients, 78%) and preauricular lymphadenopathy (30 patients, 73%). Enterovirus type 70 was isolated from four of 21 conjunctival scraping specimens. The successful isolation of the virus was due to the fact that conjunctival scrapings were obtained in the very early stage of the disease (within 48 hours) and transported immediately (within 3 hours) to the laboratory.

Acute hemorrhagic conjunctivitis (AHC) is a viral infection caused by enterovirus type 70 that can also occasionally be caused by coxsackie virus type A-24.[1,2] Characteristically, the disease has a short incubation period (8-48 hours) and lasts for 5 to 7 days. The usual signs and symptoms are pain, photophobia, foreign body sensation, copious tearing, redness, lid edema, and subconjunctival hemorrhage. Preauricular lymphadenopathy develops in most patients.[2] Fortunately it is a self-limiting disease and treatment is supportive.

An epidemic of AHC was first recognized in Ghana in 1969, at the time of the Apollo XI trip to the moon, and was therefore called "Apollo conjunctivitis."[3,4] During 1974 and 1975, outbreaks of AHC occurred in Kenya, Burma, Thailand, Taiwan, and other Asian countries.[5,6] Other epidemics of AHC have been reported from Zaire, India, Central America, London, and the United States.[7-10] To our knowledge an epidemic of AHC has not been observed in Saudi Arabia. We report on an epidemic of AHC that occurred in the south-western region of Saudi Arabia.

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Patients and Methods

Forty-one patients were examined on 4 October 1988 at the eye clinic of Gizan General Hospital. Patients were selected consecutively from those presenting to the eye clinic with symptoms of redness and pain of the eyes.

We obtained a detailed history from each patient and two of the investigators (M.F.A. and K.F.T.) examined all the patients. Each patient underwent a complete ophthalmological examination, including biomicroscopy. Regional lymph nodes (e.g., preauricular and submandibular) were palpated in all patients.

To obtain the conjunctival scrapings, topical 0.4% benoxinate was instilled into both eyes in 20 patients, and the scrapings obtained using a sterile Kimura spatula. Scrapings were obtained from both the upper and lower palpebral conjunctiva and placed on a clean dry glass slide. Specimens were fixed with absolute methanol for Giemsa staining. The spatula was then heat sterilized and a second scraping was performed. Each specimen was inoculated into a virus transport media (minimal essential media [MEM], 0.5% fetal calf serum [FCS], penicillin, streptomycin, and neomycin) and all specimens were immediately shipped to the virology department at the College of Medicine, King Khalid University Hospital, in Riyadh. Specimens were transported on ice and arrived at the laboratory within three hours of the scraping. Part of the samples were inoculated into cell cultures on the same day and the rest were kept at -20°C for later inoculation. A total of 20 conjunctival scrapings were collected from 20 patients.

Virus Isolation

The cell lines used were: MRC-5 (human embryonic lung fibroblast; Whittaker M.A. Bioproducts, U.S.A.), Hep-2 (human carcinoma of larynx; Flow Laboratories, England), and Vero (African green monkey kidney; Flow Laboratories, England). MRC-5 cells were grown in 25 cm^2 tissue culture flasks (Sterilin Ltd., England). MRC-5 cells were grown in MEM supplemented with 15% FCS and 1% flow nonessential amino acid concentrates (NEAAC), while media for Hep-2 and Vero cells contained only 10% FCS and no NEAAC. Approximately 0.5 ml of the specimen was inoculated into each tissue culture flask which had previously been washed twice with serum-free Eagle's MEM and then drained. The inoculum was allowed to absorb for one hour at 37°C and then 5 ml of serum-free MEM, as a maintenance media, was added to each flask. Flasks were incubated at 37°C and observed daily for development of cytopathic effects. If cytopathic effects did not appear after the fourth passage the isolation attempt was considered unsuccessful.

Electron Microscopy

Conjunctival scrapings were put on a carbon-coated grid and stained with phosphotungstic acid. The morphological as well as clumping patterns were examined under the transmission electron microscope.

Results

Clinical Findings

The study involved 41 patients with AHC. There were 29 (71%) males and 12 (29%) females. Twenty-one (51%) patients were under the age of 20 years. Table 1 shows the age and sex distribution of the patients studied. All patients experienced abrupt onset and the symptoms peaked within a few hours. The incubation period for all patients was less than 24 hours, and ranged from 2 to 24 hours with a mean of 16 hours. Pain and redness were the most frequently encountered symptoms and were found in all patients. Most patients complained of mild tearing with a serous to fibrinous discharge. The symptoms quickly subsided by the third or fourth day after onset. None of the patients had any associated systemic symptoms.

The subconjunctival hemorrhage varied from small and fine to patchy and diffuse. It was the most characteristic finding of the disease and was present in 32 (78%) patients. The most common feature was patchy semilunar subconjunctival hemorrhage located in the superior bulbar conjunctiva. The cornea was not affected in any patients. Preauricular lymphadenopathy was found in 30 (73%) patients. Puffiness of the eyelids was a common finding in the patients.

The right eye was affected in 29 (71%) patients first, and in only one patient were both eyes affected at the same time. Forty (97.6%) patients were right-handed, which may indicate that hand-

TABLE 1. *Age and sex distribution.*

Age (yr)	Male	Female	Total
< 10	7	4	11 (27%)
10 - 20	7	3	10 (24%)
21 - 30	3	1	4 (10%)
31 - 40	7	4	11 (27%)
> 40	5	0	5 (12%)
Total	29 (71%)	12 (29%)	41

TABLE 2. *Patients with positive viral culture.*

Age (yr)	Sex	Time of collection of specimens after onset (hr)	IP (hr)	History of contact with other patients	LN	Follicles
40	M	24	8	+	–	+
56	M	18	12	+	+	+
18	M	48	6	+	+	–
17	M	48	24	+	+	+

IP = incubation period; LN = lymph nodes.

to-eye contact was the most common route of infection. The disease affected 31 (75.6%) patients in both eyes, while the right eye was affected in only six (14.6%) and the left eye in four (9.8%) patients. Upon questioning, 39 (95%) patients indicated they had been in contact with affected persons.

Virus Isolation

Enterovirus type 70 was isolated from four conjunctival scrapings of the 20 patients (Table 2). Thirty patients had the onset of AHC within 72 hours of exposure to the affected person. All four specimens with positive viral isolation were obtained within 48 hours after the onset of symptoms. MRC-5 was the most susceptible cell line; three isolates were detected on the first passage and one on the second. All four isolates were identified as an enterovirus on the basis of their cytopathic effects in tissue culture and as enterovirus type 70 on the basis of the neutralization test and immune electron microscopy findings. None of the isolates was neutralized by anti-coxsackie 24 (Joseph; National Institute of Allergy and Infectious Diseases [NIAID]) or by anti-adeno 8 (Trim, NIAID) and 11 (Slobitski, NIAID).

Electron Microscopy

Electron microscopy showed a typical picornavirus morphological appearance. The virus had a diameter of approximately 28 nm. Immune electron microscopy demonstrated clumping of virus isolates with anti-EV70 only.

Discussion

To our knowledge, this report describes the first known outbreak of AHC caused by enterovirus type 70 to be witnessed in the Kingdom of Saudi Arabia. This epidemic is similar to those reported from other countries, including Ghana, Burma, Thailand, Taiwan, Malaysia, Singapore, Borneo, Hong Kong, New Delhi, Calcutta, Sri Lanka, the Philippines, and Japan.[3,11,12] In 1981, epidemics occurred in Nigeria, Zaire, India, Pakistan, U.A.E., Brazil, the Caribbean Islands, Central America, and southern United States.[12-14]

In all those epidemics where virus isolation was attempted, enterovirus type 70 was found as the causative agent.[14,15] The first reported isolation of enterovirus type 70 was in September 1971 in Japan.[16] The success rate of the isolation of the virus causing the conjunctivitis is very low. Many reports described lack of success in isolating a virus.[15,17,18] We succeeded in isolating the virus from four patients, and this could be due to the fact that conjunctival scrapings were obtained in the very early stages of the disease (within 48 hours) and specimens transported immediately (within three hours) to the laboratory. All specimens that were kept at -20 to -70°C yielded negative findings.

Our findings suggest that tissue culture cell line MRC-5 is a susceptible cell line for the isolation of enterovirus type 70. Enterovirus type 11 and coxsackie virus type A-24 variants have also produced AHC. Mixed epidemics caused by enterovirus type 70 and type 11 have occurred in Taiwan and Singapore, and a mixed epidemic caused by enterovirus type 70 and coxsackie virus type A-24 occurred in Hong Kong and Singapore.[19,20,21] The clinical picture resembled that of other epidemics of AHC.

The spread of infection through hand–eye contact was clear in our study, as 97.6% were right-handed and the right eye was affected first in 71% of our patients. Person-to-person contact was a factor in spreading the conjunctivitis, since 39 (95%) patients indicated that they had been in contact with a person with a history of red eyes.

Other sources of spread of infection were crowded living conditions and unhygienic practices, particularly sharing of belongings or sleeping in the same room. Ninety percent of our patients had shared their belongings with other members of their household. Good hygienic practices, as well as simple handwashing and the avoidance of material contaminated with eye discharge, may prevent the spread of infection.

AHC is a self-limiting disease, and complications can result. These include cranial nerve palsies (which are rare) and poliomyelitis.[22] None of our patients had sought any folk remedies.

Coastal areas with dense populations are the most susceptible to such epidemics. Preventive measures should be taken whenever epidemics occur. Public education is especially important.

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URINARY CALCIUM, PHOSPHATE, AND URIC ACID EXCRETION BEFORE AND AFTER STONE SURGERY

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قورنت مقادير الكالسيوم والفسفات وحمض اليوريك المفرزة مع البول خلال ٢٤ ساعة لدى مجموعتين من المرضى الذكور قبل العلاج الجراحي للحصيات الكلوية وبعده. ضمت المجموعة أ ٣٩ مريضًا أجري لهم استخلاص جراحي تام للحصيات، وضمت المجموعة ب ١٥ مريضًا لديهم حصيات ثمالية. جمعنا كميات البول المفرزة خلال ٢٤ ساعة من كل مريض قبل إزالة الحصاة وبعدها. بالنسبة للمجموعة أ ارتفع متوسطا الكالسيوم والفسفات (± الخطأ العياري للمتوسط) بدرجة مهمة (P < ٠,٠٥) بعد الجراحة ولكن مستويات حمض اليوريك لم تتغير بدرجة مهمة. أما بالنسبة للمجموعة ب فإن متوسطات الكالسيوم والفسفات وحمض اليوريك (± الخطأ العياري للمتوسط) لم تكن تختلف بدرجة مهمة (P > ٠,٠٥) عما كانت عليه قبل العملية. وتشير نتائج هذه الدراسة إلى كون مقادير الذوائب في البول قبل العملية منخفضة على نحو مضلل وذلك بسبب إشغال الذوائب البولية في عملية تكوين الحصيات. وبناء على ذلك ينصح بقياس مقادير الكالسيوم والفسفات وحمض اليوريك المفرزة مع البول خلال ٢٤ ساعة بعد الإزالة الجراحية التامة للحصيات وربما انطبق ذلك على عوامل الخطورة الأخرى لأن الافراز البولي من هذه الذوائب لن يتأثر عندئذ بوجود الحصيات في الكلى.

In a prospective study, 24-hour urinary excretions of calcium, phosphate, and uric acid were compared in two groups of male patients with renal stones before and after surgical treatment. Group A comprised 39 patients who had complete surgical clearance of the stones. Group B consisted of 15 patients with residual stones. 24-Hour urinary collections were obtained in each patient before and after stone removal. In Group A, the mean (± SEM) urinary excretions of calcium and phosphate rose significantly ($P < 0.05$) after surgery but uric acid levels did not change significantly. In Group B, the mean (± SEM) postoperative urinary excretions of calcium, phosphate, and uric acid were not significantly different ($P > 0.05$) from preoperative values. The findings in this study suggest that, in view of the utilization of these urinary solutes in the process of stone growth, preoperative urinary estimation is misleadingly low. It is therefore advisable to carry out the 24-hour urinary estimations of calcium, phosphate, uric acid, and perhaps other risk factors only after complete surgical clearance of the stones, because at this time urinary excretion of these solutes will not be modified by the presence of the stones in the kidneys.

During the last decade, adoption of less invasive modalities for the treatment of renal stones has modified the therapeutic strategies. Complicated and recurrent stones can now be removed with less accompanying morbidity and mortality.[1] Nevertheless, the value of estimating urinary calcium, uric acid, oxalate, phosphate, magnesium, and other urinary constituents is still emphasized, not only in patients with recurrent stones but also in those with single episodes of stones.[2,3] Patients with hyperuricosuria, for instance, are reported to excrete higher levels of calcium and to have more severe stone disease in terms of stone removal operations.[4] The process involved in urinary stone nucleation and growth includes consumption of substances known as risk factors.[5] When these

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processes are operant, urinary estimations of the solutes may be misleadingly low and hence may not accurately reflect the physiological state that initiated the calculogenesis. The present study was designed to compare excretion of some urinary solutes before and after complete and incomplete surgical urinary stone clearance.

Patients and Methods

Fifty-four male patients with radiologically confirmed renal stones were included in this prospective study. All were admitted to Asir Central Hospital in Abha for stone removal surgery and underwent urinary studies while on an ordinary hospital diet with no calcium restriction. Urinalysis, urine culture, blood urea and electrolytes, serum creatinine, serum calcium, serum uric acid, serum phosphorus, and complete blood count were done. All patients underwent intravenous urography to ensure that both kidneys were functioning.

Fifteen patients had 24-hour urine collection twice before surgery and the rest had it only once before surgery but all had it once again after operation and before discharge (usually on 10th to 14th days). Voided urines were kept at 4°C until delivery to the hospital laboratory immediately after completion of collection. The 24-hour urine volume was measured and an aliquot was taken and kept frozen until the estimations of solutes were done. Most patients underwent open surgery for stone removal, but a few had endoscopic stone removal done by percutaneous nephrolithotomy. All patients had a plain x-ray study of the kidney, ureter, and bladder to verify completeness of stone removal before discharge. Intravenous urography was performed on the first follow-up visit, 4 to 6 weeks after discharge. Patients were separated into two groups: Group A comprised 39 patients who had complete clearance of the stones and Group B consisted of 15 patients who had residual stones. Ten patients in Group A and seven patients in Group B were readmitted and had another 24-hour urine collection at the time of follow-up. Calcium, phosphate, and uric acid levels were estimated in all urine collections. Calcium content was estimated in all urine collections and was estimated by the manual method using *o*-cresolphthalein complexone without deproteinization. The phosphate level was estimated from the reaction of phosphate with molybdate using a Gemstar analyzer. The uric acid concentration was estimated using the enzymatic calorimetric method of the Gemstar analyzer. The stones removed from the patients were chemically analyzed qualitatively using an Oxford reagent set (Lancer, Athy Co., Kildare, Ireland). Statistical comparisons of the mean ± SEM of the preoperative and postoperative values were made using Student's *t* test.

Results

Both groups were matched for age (Group A mean, 39.2 yr; Group B mean, 40.1 yr). The mean values (± SEM) of the average of estimated calcium, phosphate, and uric acid excretion in the two 24-hour preoperative urine collections in the 15 patients did not differ significantly from the estimated values in either of the single preoperative 24-hour urine specimens collected from the same patients.

Urinary Calcium, Phosphate, and Uric Acid Levels in Group A

The preoperative mean urinary calcium level was 3.97 ± 0.29 mmol/day and postoperatively rose significantly to 5.57 ± 0.56 mmol/day ($P < 0.05$) (Figure 1). The preoperative urinary phosphate excretion was 17.3 ± 1.14 mmol/day and postoperatively increased significantly to 22.83 ± 1.57 mmol/day ($P < 0.05$) (Figure 2). The preoperative mean urinary uric acid level was 3.06 ± 0.24 mmol/day and postoperatively rose to 3.42 ± 0.19 mmol/day after surgical clearance of stones, but the difference was not significant ($P > 0.05$) (Figure 3).

Urinary Calcium, Phosphate, and Uric Acid Levels in Group B

The 24-hour urinary calcium, phosphate, and uric acid levels were estimated at the follow-up visit in ten Group A patients and seven Group B patients, and levels did not differ significantly from the postoperative urinary values recorded before discharge. The preoperative mean urinary calcium level was 3.7 ± 0.72 mmol/day and postoperatively did not differ significantly—3.86 ± 0.87 mmol/day (see Figure 1). Mean urinary phos-

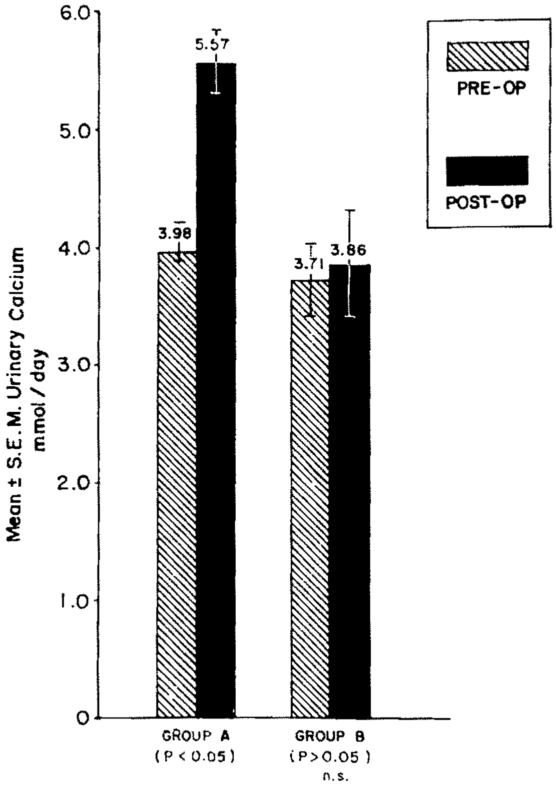

FIGURE 1. Comparison of preoperative and postoperative urinary calcium levels between Group A and Group B patients.

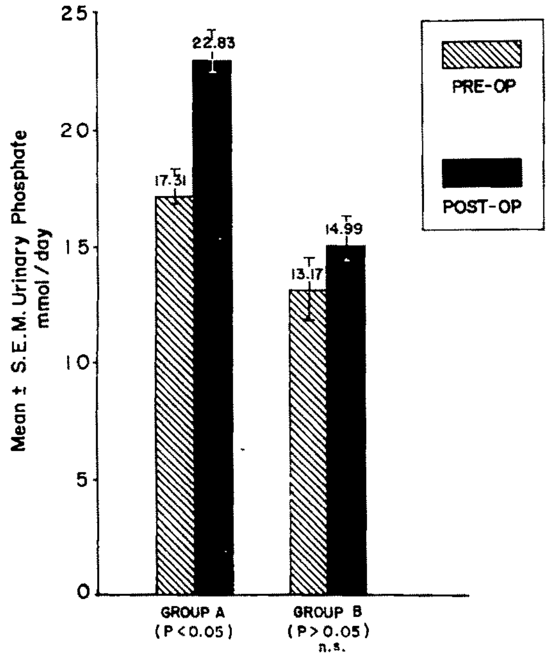

FIGURE 2. Comparison of preoperative and postoperative urinary phosphate levels between Group A and Group B patients.

phate content was 13.17 ± 2.77 mmol/day preoperatively and rose to 14.99 ± 1.99 mmol/day postoperatively but the difference was also not significant ($P > 0.05$) (Figure 2). Mean urinary uric acid concentration before surgery was 2.66 ± 0.29 mmol/day and was 3.2 ± 0.42 mmol/day postoperatively with no significant change (see Figure 3).

Chemical Analysis of Stones

In Group A, the stones in 37 of 39 (95%) patients contained calcium, 27 (70%) contained phosphate, and 20 (51%) contained uric acid. In this group, there were three (8.33%) infected stone formers. In Group B, 13 of 15 (87%) contained calcium, 11 (73%) contained phosphate, and only 6 (40%) contained uric acid. There was one (7.1%) infected stone former in this group. The ratios of infected to noninfected stone formers in Groups A and B are comparable.

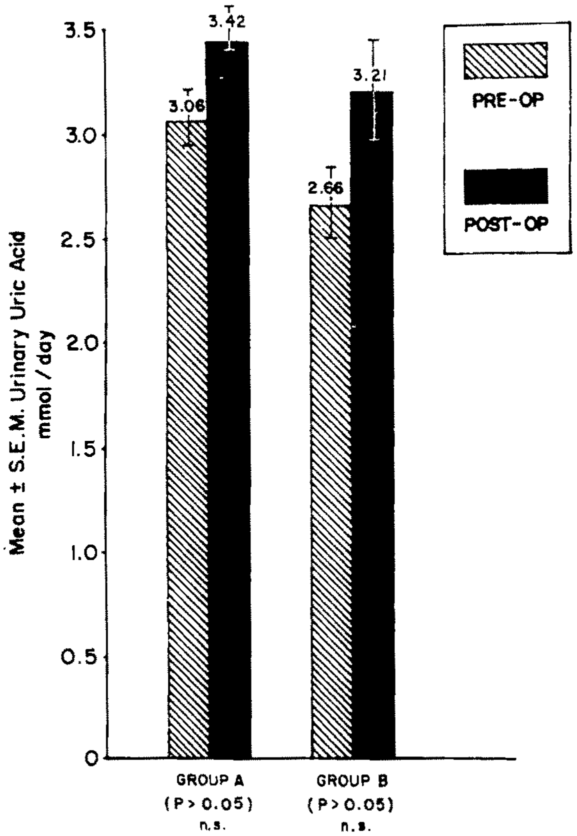

FIGURE 3. Comparison of preoperative and postoperative urinary uric acid levels between Group A and Group B patients.

Discussion

In a previous study it was found that urinary uric acid levels were significantly less in a group of hyperuricemic patients with urinary uric acid stones compared with a control group of normal subjects.[6] It was postulated that, in view of the relationship of urinary uric acid consumption to stone formation and growth, the amount recovered in urine before complete stone removal may become misleadingly lower than expected. The present investigation examined this hypothesis and also considered the urinary calcium and phosphate levels before and after stone clearance.

Mechanisms of urinary stone formation are still a subject of controversy. The physicochemical theory of urinary supersaturation ignores the role of matrix in calculogenesis.[7-9] On the other hand, the "matrix" theory emphasizes the role played by the matrix in the initiation of urinary stone formation and assumes that minerals are then merely incorporated by a process of encrustation.[10,11] Nonetheless, no matter which theory is correct, it is doubtless that eventually urinary constituents such as calcium, phosphate, oxalate, uric acid, and magnesium will be consumed to accomplish stone growth. Study of 24-hour urinary excretions of these risk factors is essential and should be evaluated even in patients with a single stone.[12] It is conceivable that estimations of these urinary constituents in patients harboring stones could be misleadingly low in view of the continuing stone growth. Indeed, in Group A patients of this study, the mean (± SEM) levels of urinary calcium and phosphate rose significantly ($P < 0.05$) after complete surgical clearance of the stones. However, the urinary uric acid levels did not rise significantly, perhaps because only 50% of the stones in this group contain uric acid. Ninety-five percent of the urinary stones in this group contained calcium and 70% contained phosphate. It could be argued that the postoperative rise is due to the seasonal and diurnal variations that have been observed in stone formers and normal subjects.[13-15] It is difficult to agree with this view because the reported significant postoperative rise in calcium and phosphate did not occur in Group B patients who had residual stones after surgery. Indeed the mean levels of urinary calcium, phosphate, and uric acid in Group B were not significantly different after surgery compared with preoperative values.

It could also be argued that the significant postoperative rise in urinary calcium and phosphate levels in Group A patients exceeds what could be explained solely on the basis of consumption of these minerals to achieve stone growth before surgery. Therefore it might be said that the rise was purely dietetic, perhaps because the patients in this group felt better after surgery, ate more, and simply excreted these minerals in abundance in their urine. If this were true, there should also be a similar significant rise in urinary uric acid after surgery, since it is also known to be affected by diet. However, this did not occur in Group A. Furthermore, it is unlikely that the patients in Group B did not exhibit a significant postoperative rise because they did not feel or eat well enough in view of their residual stones, as the patients in Group B were totally asymptomatic after surgery, did not have longer hospitalizations, and felt as well as the patients in Group A. Their residual stones were discovered only accidentally on postoperative x-ray studies.

The patients under study were not put on a calcium-restricted diet but received an unrestricted hospital diet. This approach is recommended whenever urinary studies are carried out so that ordinary daily life conditions of the patients will be reflected.[3] Preoperative 24-hour urine collections were obtained twice in 15 patients and the average of the two readings of calcium, phosphate, and uric acid levels was compared with the readings in each single collection. Two collections were taken because of reported findings that discourage reliance on one 24-hour urine collection.[3,16] However, we found no significant difference between the mean of the average of estimations in the two 24-hour urine collections versus the mean in the single collections, so decided that single 24-hour collections would be reliable in the remaining patients.

It is conceivable that, in the immediate postoperative period, urinary excretion of calcium, phosphate, and uric acid may be modified by the metabolic and endocrine changes known to occur after surgery. Performing these investigations on urinary risk factors in stone formers after a minimum of 3 months following a renal colic episode or surgery has been recommended.[17] However, by that time patients, for fear of further stone formation, may have modified their diet and fluid intake so that urinary values are affected—a condition which has been called "the stone clinic effect."[18] In the present study, the postoperative estimations were carried out when the patient was freely ambulant and just before discharge, usually after 10 to 14 days from the time of operation. The effect of the metabolic and endocrine changes could be minimal at this time. Indeed, when the 24-hour urine estimations were repeated after 4 to 6 weeks on ten patients from Group A and seven patients from Group B, results did not differ significantly from the postoperative values obtained before discharge.

In urolithiasis, urinary calcium and phosphate levels increase significantly after complete stone removal. Other constituents such as oxalate, although not studied, may behave similarly. Because preoperative urinary estimation of these constituents could be misleading, this biochemical assessment should be delayed until complete surgical stone clearance is accomplished. It might even be better if it is carried out after discharge from the hospital, during postoperative follow-up, to allow time for the metabolic and endocrine postoperative changes to return to normal. However, it should not be delayed for a long time, to avoid the "stone clinic effect."

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Special Communication

EVALUATION OF NEWBORN CARE IN THE KINGDOM OF SAUDI ARABIA: A FIRST STEP TOWARD REGIONALIZATION OF PERINATAL CARE

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تم في عام ١٩٨٥م تقييم مرافق رعاية الولدان وأنظمتها وحجم المرضى في مراكز الولادة والأطفال في المملكة العربية السعودية كخطوة أولى نحو توفير البيانات التي قد تلزم لإعداد خطط التوزيع الجغرافي المثلى لهذه المراكز، من خلال مسح ١١٠ مراكز في ٥٢ مدينة وقرية باستخدام طريقة التقييم في الموقع. تدير وزارة الصحة ٦٠ مركزا (٥٥٪) وتعتبر بذلك من أكبر القائمين على توفير الرعاية الصحية، بينما يرتبط ٣٣ مركزا (٣٠٪) بالقطاع الخاص. وتدير القوات المسلحة والجامعات وغيرها من الجهات الحكومية ١٧ مركزا (١٥٪). كان الإجمالي السنوي للمواليد الأحياء في مراكز الولادة والأطفال في مناطق المملكة المختلفة. لا يقدم سوى عدد قليل من مراكز المستوى الثالث برامج تثقيفية خارجية أو مساعدة في نقل الولدان. هناك نقص في أعداد الهيئة الطبية والتمريضية لرعاية الولدان. وقد ألقت هذه الدراسة الضوء على أهمية البيانات في مسألة التوزيع الجغرافي لخدمات رعاية الولدان في المملكة.

The newborn care facilities, policies, and patient load in the perinatal care centers (PNCCs) in Saudi Arabia were assessed in 1985 as a first step toward providing data that would be needed in formulating plans for the optimal regionalization of perinatal care. A total of 110 PNCCs based in 52 towns and villages were surveyed using on-site evaluation. The Ministry of Health, with 60 (55%) of the 110 PNCCs, is the major health care provider, while 33 (30%) belong to private organizations. The Armed Forces, universities, and other government agencies account for 17 (15%). There was an annual total of 212,048 live births in the PNCCs. Except for variability in the distribution of Level III centers, there was good correlation between the number of live births per year and the number of PNCCs in the different parts of the Kingdom. Few of the Level III centers provide outreaching educational programs or assist in neonatal transportation. A shortage of medical and nursing staff for neonatal care was found. The importance of the data for regionalization of perinatal care in the Kingdom is highlighted.

Over the last two decades, the Kingdom of Saudi Arabia has experienced tremendous development in many areas, including that of health care. Perinatal and neonatal health care have been part of this general trend toward development and improvement. Optimal utilization of neonatal care resources requires appropriate coordination between the available neonatal health care facilities. The objective of such coordinated care is to provide appropriate health care for every newborn infant, according to the severity of illness, in order to reduce perinatal and neonatal morbidity and mortality. Many of the neonatal care units in the Kingdom are currently providing services ranging from Level I to Level III, without any clearly coordinated approach.[1] Thus, organized communication and back-up support between the various neonatal care units are missing in most cases. This is reflected in the wide variation of perinatal and neonatal statistics from various units in the Kingdom[2,3] and can lead to unnecessarily

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large numbers of neonatal deaths and neurological defects among survivors.

There is a need for a model to coordinate existing neonatal health care facilities in the Kingdom, with the objective of better utilization of available resources. Good examples of such a model are the regionalized perinatal health care services of North America and some European countries, where hospitals with perinatal care facilities in a specified region are classified into three levels, I to III, each with defined functions and responsibilities.[4] Good communication and support between the various levels of centers, plus adequate transportation services, will assure smooth continuity of patient care and improve pregnancy outcome.[5]

Considering the geography and demography of Saudi Arabia, and the current situation of neonatal health care, development of a program of regional perinatal health care would improve the outcome of pregnancy through better utilization of available resources. The fundamental steps of a program of regionalization would include a planning phase, followed by an implementation phase.

Components of the planning phase would include: (1) regional surveys to ascertain demography, geography, climate, and the relation of obstetric and pediatric units to existing hospitals; (2) assessment of available perinatal care facilities with regard to number of beds, equipment, manpower, and physical facilities; (3) planning for the effective regional administration of perinatal care services; (4) organization of lines of communication; and (5) organization of transportation services.

The implementation phase would require specific operational objectives which should include correction of identified deficiencies to improve the quality of care, formulation of criteria for transfer within a region, and development of support-systems for consultation, laboratory services, educational programs, and transportation. The implementation phase should also include continuous assessment and review of the program.

Applying this scheme for a regionalized system of perinatal care, we conducted a national survey of neonatal resources and patient loads in the Kingdom during 1985. We present some of the data from this national study which can serve as a foundation for a realistic regionalization plan for the Kingdom.

Material and Methods

All neonatal care units in the Kingdom were surveyed as to physical facilities, equipment, staffing, policies, and other relevant variables, including hospital births, by means of an extensive questionnaire[1] with more than 600 items. This questionnaire was completed by trained surveyors onsite in each facility. Each neonatal care unit was then designated as providing one of three levels of care.[4]

Level III perinatal care facilities are referral centers, frequently teaching hospitals, that serve as back-up for linked Level I and II facilities. All pregnancy and neonatal disorders are managed in Level III facilities. These centers should therefore provide transportation for sick newborns as well as outreaching educational programs. Research and participation in regional perinatal organization are other important functions of Level III centers.

Level II centers are large community hospitals that deal with most disorders of the newborn and in some cases can manage those treated in Level III centers. The availability and geographic location of Level III centers in a region are factors that influence the resources available in Level II units.

Level I centers deal only with normal deliveries and newborns, and refer high-risk obstetric patients to Level II and III centers, but should be staffed and equipped to handle unexpected emergencies, such as immediate resuscitation.

To determine the location, administration, and type of care provided by the institutions surveyed, we assessed the distribution of hospitals by region, organization, and level of neonatal care. Similarly the regional distribution of annual hospital deliveries, manpower resources, and physical facilities was determined to assess patient loads and resources.

With the Kingdom's estimated population of 10 million and crude birth rate of 45.9 per 1000 population,[6] the expected number of total births for each region was calculated and the percentage of out-of-hospital births was estimated. The available manpower and physical resources found in each region were also compared with data published.[4]

Results

In the eleven regions of the Kingdom, as classified by the Ministry of Health, there were 110 hospitals or medical centers providing neonatal care in 52 towns and villages. All are well connected by modern roads and highways. Air routes also connect most of these towns and villages (Figure 1).

Sixty hospitals (55%) of the 110 neonatal care facilities are Ministry of Health hospitals. Other important health care providers in the Kingdom include the armed forces hospitals (military, National Guard, Security Forces), which account for 10% of facilities; the private sector, accounting for 30%; and universities and other government agencies, accounting for 5% (Table 1). According to the level of perinatal care provided, 16 hospitals were classified as Level III, 75 as Level II, and 19 as Level I. Only four of the 60 Ministry of Health hospitals were classified as Level III, whereas six of the eleven armed forces hospitals provide Level III care.

Survey of the regional distribution of perinatal facilities revealed that five regions lack hospitals with Level III neonatal care services, although the overall ratio of the number of such units to total hospital births in the Kingdom is satisfactory (Table 2). Important elements, including back-up support and transportation of patients from referring hospitals, outreaching educational programs, and participation in regional perinatal organization, are lacking in most of the Level III hospitals.

The regional distribution of perinatal care load (population, annual hospital births, estimated

TABLE 1. *Levels of neonatal care facilities by organization in Saudi Arabia.**

Organization	Level I	Level II	Level III	Total
Ministry of Health	12	44	4	60
Private	7	24	2	33
Armed forces	0	5	6	11
University	0	1	3	4
Government	0	1	1	2
Total	19	75	16	110

* See text for definitions of the three levels of neonatal care facilities.

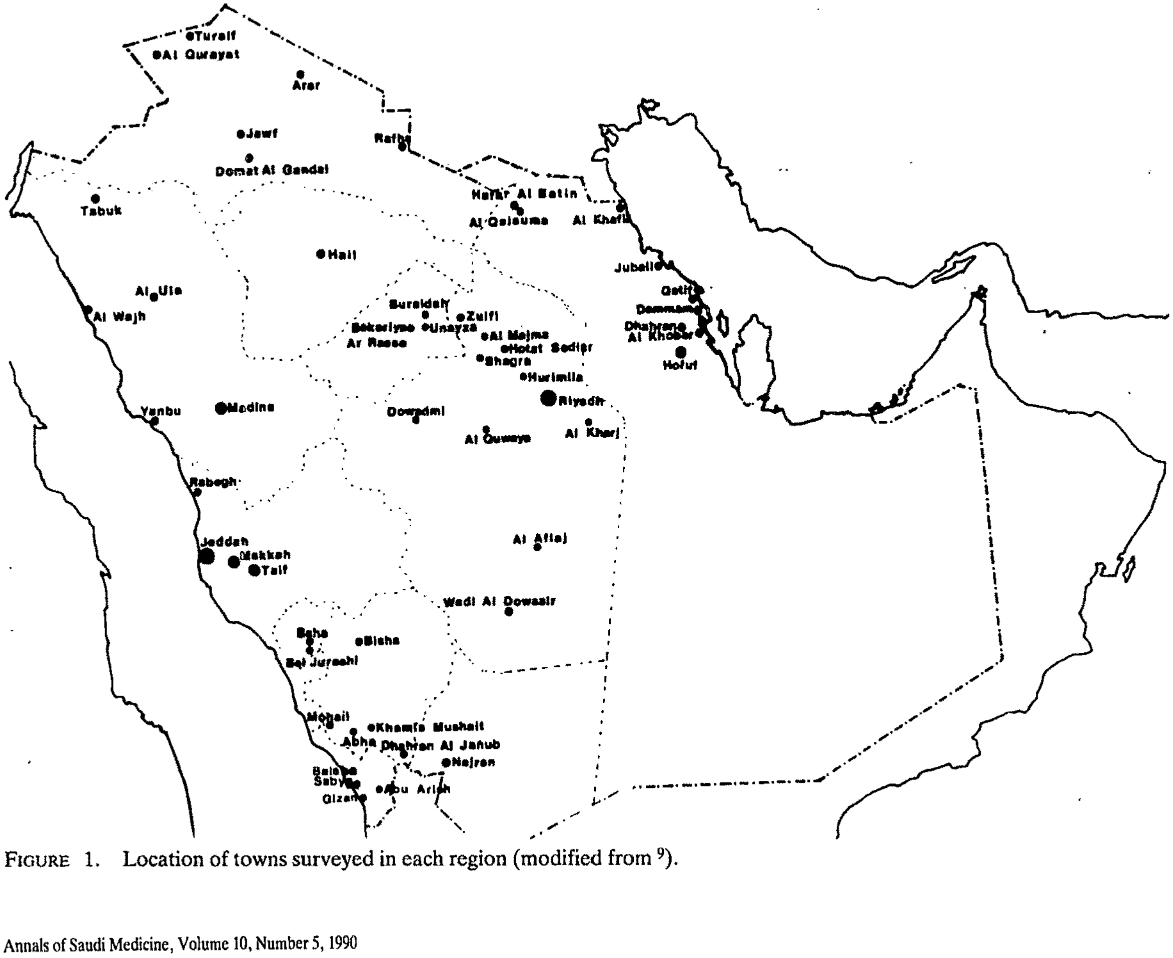

FIGURE 1. Location of towns surveyed in each region (modified from [9]).

TABLE 2. *Regional distribution of births and neonatal care facilities in Saudi Arabia.*

Region	Live births	Level I	Level II	Level III	Total centers
Riyadh	55,248	8	15	4	27
Mecca	57,765	4	17	5	26
Baha	3,937	0	1	1	2
Medina	23,744	1	7	2	10
Eastern Province	32,779	2	13	2	17
Asir	11,820	0	4	2	6
Najran	2,575	0	2	0	2
Gizan	4,071	1	4	0	5
Gasim	8,063	0	4	0	4
Northern Province	9,009	3	6	0	9
Hail	3,037	0	2	0	2
Total	212,048	19	75	16	110

* See text for definitions of the three levels of neonatal care facilities.

TABLE 4. *Neonatal special care resources in Saudi Arabia in 1985.*

Resources	Available	Expected	Percentage of coverage
Beds[a]	907	846* 1763†	100* 51†
Neonatologists[b]	55	75* 144†	73* 38†
Residents[c]	51	180* 350†	28* 15†
Nurses	254 (1:3.5 nurse/pt)	432* 881† (1:2 nurse/pt)	58* 29†

* For current hospital deliveries; † for estimated total deliveries.

[a]Estimated as 6 NNSC beds/1000 live births; [b]one per 10 NNSC beds; [c]one per 5 NNSC beds.

NNSC = neonatal special care.

total annual births) and resources (hospitals with perinatal care facilities, number of obstetric beds, neonatal special care [NNSC] beds, and number of obstetricians and pediatricians) in Saudi Arabia for the year 1985 are summarized in Table 3. There was good correlation between the population and expected number of live births per year and the distribution of perinatal care centers in different parts of the Kingdom. However, there was an uneven regional distribution of obstetric and NNSC beds. Hospital deliveries constituted only 46% of the estimated total number of deliveries in the Kingdom, with the remainder out of hospital deliveries. The regional distribution of hospital births as a percentage of the estimated total births shows wide variation, ranging from as low as 15% in the Gizan region to as much as 66% in the Riyadh region.

The number of NNSC beds available is sufficient for the number of hospital deliveries, but represents only 51% of the number needed for the expected total annual deliveries in the Kingdom (Table 4). The number of residents working in the various neonatal special care units represents only 28% of the number needed for NNSC beds, using the recommended ratio of one resident per five NNSC beds.[4] Similarly, the number of nurses assigned per shift to the available NNSC beds represents only 58% of the number needed for these beds, based on a ratio of one nurse per two NNSC beds on each shift.[4]

Analysis of the space allotted to the intermediate and intensive care areas in the various

TABLE 3. *Regional distribution of perinatal care load and resources* in Saudi Arabia (1985).*

		Regional distribution as percentage of total										
Variable	Total number	Riyadh	Makkah	Baha	Medina	Eastern Province	Asir	Nejran	Gizan	Gasim	Northern Province	Hail
Population	10m	18.0	25.0	2.7	10.2	10.9	9.7	2.1	5.8	4.6	3.2	3.7
Hospitals	110	24.5	23.6	1.8	9.1	15.5	5.6	1.8	4.5	3.6	8.2	1.8
Obstetric beds	3,696	28.4	25.3	1.5	14.9	14.2	3.2	1.0	2.0	4.7	2.4	2.4
NNSC beds	907	28.0	22.0	5.0	7.0	19.0	4.0	1.7	1.7	4.6	5.0	2.0
Hospital births*	212,048	26.2	26.1	1.9	11.2	15.4	5.6	1.2	2.9	3.8	4.3	1.4
HB/EST. TB (%)	46.0	66.0	40.0	32.0	50.0	65.0	26.0	26.0	15.0	37.0	61.0	17.0
Obstetricians	451	29.7	25.5	1.8	6.4	17.5	4.2	0.7	4.0	4.7	2.4	3.1
Pediatricians	428	26.2	30.2	2.3	7.7	16.8	3.7	0.7	4.0	2.1	3.0	3.3

* Calculated expected total births for the Kingdom = 459,000.[6]

M = million; NNSC = neonatal special care; HB/EST. TB = observed hospital births/estimated total births.

TABLE 5. *Space and equipment facilities in neonatal special care units in Saudi Arabia.*

Facility	% Availability or level of adequacy
Phototherapy	92
Cardiopulmonary monitoring	58
Ventilators	49
Oxygen analyzer	45
Transportation equipment	32
Washbasin	60
Space requirement	35
Oxygen outlets	7
Electrical outlets	6
Suction outlets	5
Compressed air outlets	4

* Compared with published recommendations.[4]

Level II and Level III neonatal care units showed that only 35% of these units satisfied the space requirements of 4.5 square meters per infant and nine square meters per infant in the neonatal intermediate and intensive care areas, respectively.[4] Most of the surveyed neonatal care units also lacked the optimum number of electrical, oxygen, compressed air, and suction outlets (Table 5). Oxygen analyzers were used in only 45% of the Level II and III neonatal care facilities.

Discussion

This report assesses the current status of newborn care facilities in Saudi Arabia, which is essential for planning regionalization of perinatal care. The survey revealed that neonatal care facilities are widely distributed throughout the Kingdom, with variable levels of care provided and rapid growth of available facilities. Since completion of our 1985 survey, the number of hospitals providing neonatal health care in Saudi Arabia has increased from 110 to 178, located in 94 (previously 52) towns and villages (Table 6). The Ministry of Health is still the major provider of neonatal health care, but most of the current Level III perinatal care centers are in armed forces and university hospitals. Thus, there is a need for upgrading some Ministry of Health hospitals in some geographical areas and for cooperation among organizations providing perinatal care. This should be part of the problem addressed during the implementation phase of regionalized care.

It is essential to correct deficiencies with respect to physical structure, equipment, and manpower resources in order to improve care and avoid overcentralization. Some of the deficiencies reflect a lack of adequate knowledge of the requirements of neonatal care. It is therefore mandatory to involve neonatologists or pediatricians with knowledge and interest in the care of newborn infants in the planning stage of care facilities, since the later correction of problems, which may require major construction, is difficult in a functioning neonatal intensive care unit.

Live-birth distribution is a fundamental consideration in predicting the volume of patients requiring various levels of care in each region.[7] There is a relatively high percentage of out-of-hospital deliveries in many regions of the Kingdom, and this should be recognized when calculating the regional perinatal care loads. Other variables, such as low-birth-weight rates, also need to be determined, and a project to do so is in progress.

Since it is not economical or feasible for all PNCCs to provide Level III care, a regionalization plan must be developed that ensures appropriate care is provided, including adequately equipped facilities staffed by well-trained personnel. As reported by other authors,[5,8] this should contrib-

TABLE 6. *Current status of the number and location of perinatal care facilities in Saudi Arabia (1988).**

Variable	Riyadh region	Makkah region	Al-Baha region	Medina region	Eastern Province	Asir region	Nejran region	Gizan region	Gasim region	Northern Province	Hail region	Total
No. of Towns												
1985	11	4	2	5	9	5	1	4	4	6	1	52
1988	14	10	4	11	9	13	2	7	10	7	7	94
No. of Hospitals												
1985	27	26	2	10	17	6	2	5	4	9	2	110
1988	33	43	4	18	25	16	4	8	11	8	8	178

* Complementary study of Project AT–6–21.

ute to a reduction in the observed high perinatal mortality rate of 30.4 per 1000 total births and the neonatal mortality rate of 22.4 per 1000 live births observed during the study period. The next step toward achieving such a goal would be the establishment of regional planning bodies that would determine regional perinatal care needs, taking into consideration the available baseline data provided and addressing some of the problems identified here. These areas for improvement include more efficient transportation and communication facilities.

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Surgical Communication

ONE-STAGE PENILE AND URETHRAL RECONSTRUCTION — A NEW EXTENSION OF INFERIORLY BASED RECTUS ABDOMINIS MYOCUTANEOUS FLAP

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The loss of a penis, either through trauma or other causes, is psychologically and physiologically intolerable for the victim. The ideal reconstruction should be a reliable single-stage procedure that requires minimum hospitalization and yields acceptable cosmetic and functional results. The traditional techniques, which use tube flaps, are three- to five-stage procedures that are time consuming and physically and economically difficult for the patients.[1]

The rectus abdominis myocutaneous flap has gained popularity for various reconstructive procedures, including coverage of the groin,[2] thigh,[2] and above-knee amputation stumps.[3] Recently it has been used for vaginal and pelvic reconstruction.[4] We have used an inferiorly based rectus abdominis myocutaneous flap to reconstruct an amputated penis and urethra as a single-stage procedure.

Surgical Report

A six-year-old boy was referred to our unit for possible reconstruction for his knife-amputated penis, inflicted two years earlier by his psychologically disturbed mother. He was operated on twice at his local hospital, but no details of these attempted procedures were available.

Examination revealed absence of the penis, with the urethral opening flush with the scrotum, which was normal (Figure 1). There were irregular scars over the upper medial aspects of both thighs and the groin, suggesting that a gracilis myocutaneous flap had been attempted previously. A micturating cystourethrogram showed a truncated urethra (3 cm), with a short stricture posteriorly.

The patient was subsequently operated on using an inferiorly based rectus abdominis myocutaneous flap.

At operation a suprapubic puncture cystostomy catheter was first introduced. The right rectus muscle was used as the source of the flap. A vertical skin strip (3 × 12 cm) extending from 3 cm below the xiphoid process to 3 cm below the umbilicus was marked and an incision made down to the anterior rectus sheath, which was incised vertically at the medial and lateral borders of the rectus (Figure 2). This area was then divided at the upper border of the flap and the superior epigastric artery ligated. The whole muscle was freed from the posterior rectus sheath and dissected downward, with the attached skin, care being taken not to injure the inferior epigastric artery.

At the level of the inferior border of skin, fascia was separated from the muscle pedicle and the muscle further dissected down. Subcutaneous dissection in the suprapubic area was done and a tunnel was created, through which the flap was rotated and passed underneath to the recipient area (Figure 3). The skin was folded and sutured with interrupted 4-0 chromic catgut to reconstruct the urethra. The proximal end was anastomosed to the urethral opening after appropriate fashioning and a No. 10 Foley catheter was introduced down to the bladder as a stent.

The distal end of the skin was folded back dorsally to shape the glans penis (Figure 3). The borders of the rectus were approximated ventrally over the attached skin urethral tube using 3-0 chromic. The raw rectus muscle was covered by a

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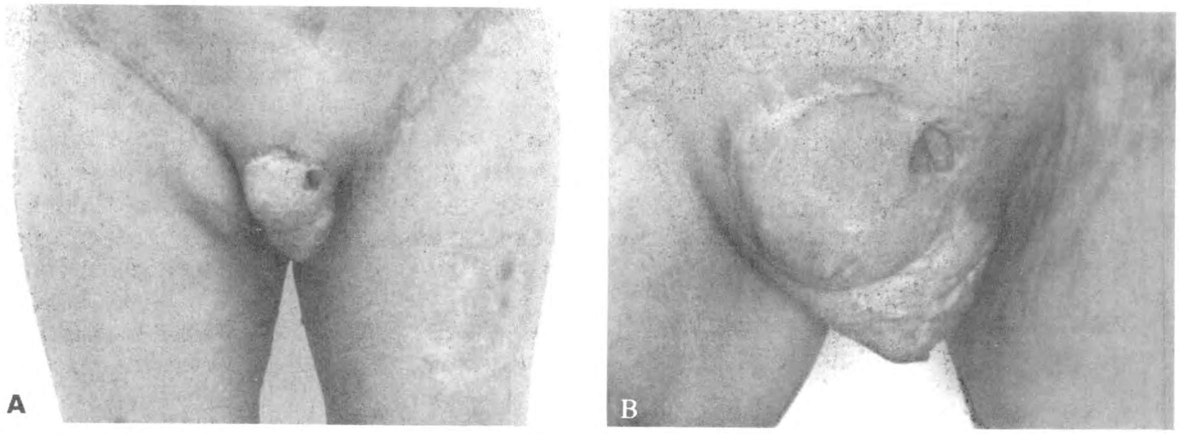

FIGURE 1. (A) The amputated penis, showing bilateral old inguinal scars from previous surgery. (B) Close-up view, showing the amputated penis almost flush with the scrotum.

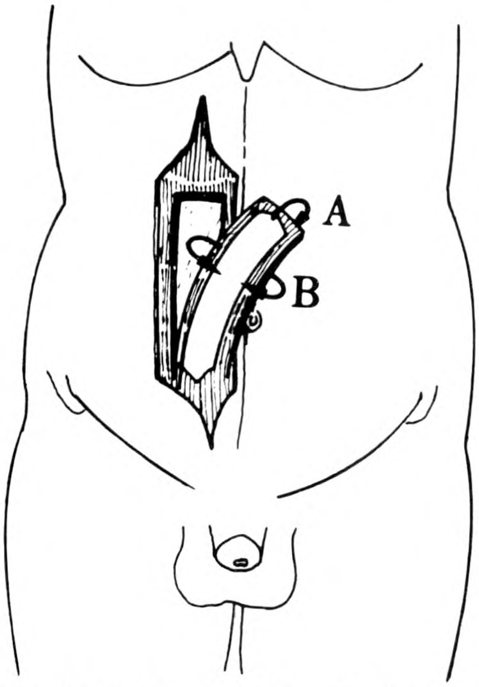

FIGURE 2. The raised strip of skin attached to the right rectus muscle.

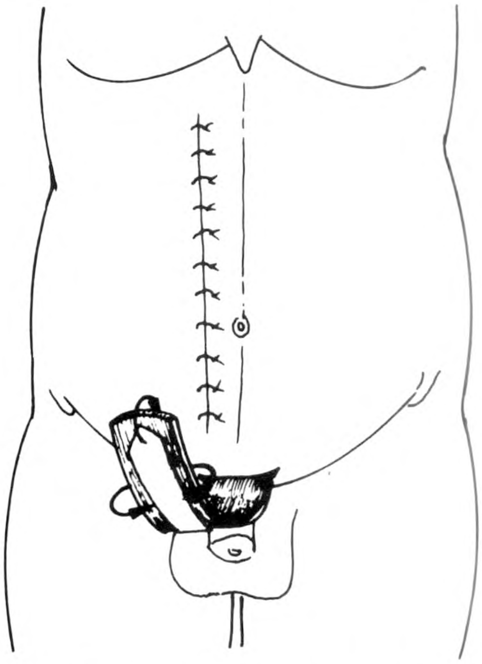

FIGURE 3. Flap brought down to recipient area through a suprapubic tunnel.

split medium-thickness skin graft taken from the thigh.

Closure of the abdominal wound was done by approximating the anterior rectus sheath fascia with 2-0 Prolene continuous suture, enforced with some interrupted sutures.

The patient's postoperative course was smooth, except for the occurrence of minor scattered patches of raw areas where the graft did not take due to seroma formation, but these eventually healed. The Foley catheter was accidentally removed 8 days postoperatively but was easily reinserted. It was electively removed two weeks after operation. The suprapubic catheter was clamped three days after removal of the Foley catheter and eventually taken out when the boy was voiding normally (Figure 4).

A postoperative micturating cystourethrogram showed unobstructed passage through the new urethra and no fistula formation, but the small

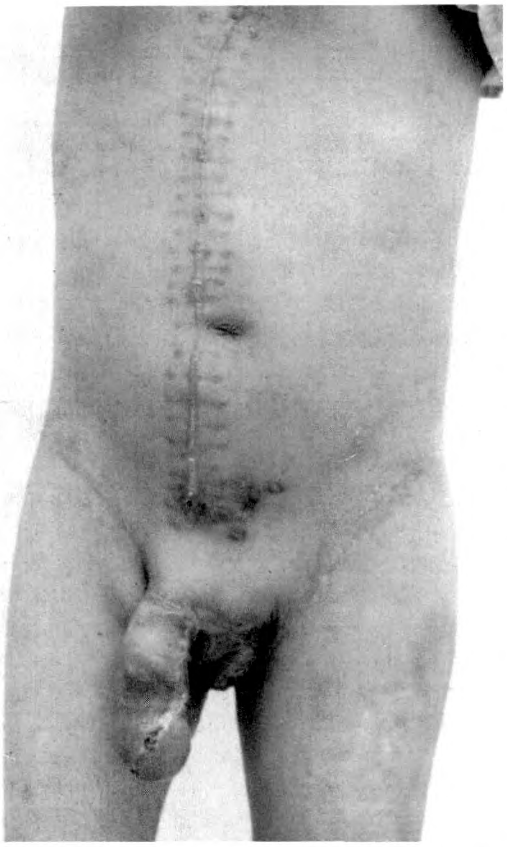

FIGURE 4. Three-week postoperative appearance of the reconstructed penis and abdominal scar.

posterior stricture remained. The boy was discharged 25 days postoperatively and by that time showed complete healing. At follow-up 6 months later, there was no abdominal weakness, difficulty in passing urine, or marked atrophy of the flap, which remained firm but big for his age.

Discussion

A standard procedure for penile reconstruction does not exist, but many are available. The multistage tube flaps are not acceptable by many surgeons today. Gracilis muscle or a myocutaneous flap[5,6] may not be available due to previous failed attempts to use this material, as in our patient. Sometimes the patient's condition is complicated by the effects of previous radiation therapy to the groin. Mathes and Nahai[7] reported that the frequency of loss for rectus abdominis myocutaneous flaps ranked among the lowest, while gracilis myocutaneous flap loss ranked among the highest. The microsurgically performed free forearm flap procedure, with cartilage insertion, has also been used.[1] It has probably yielded the best functional and aesthetic results, but it is not easy to perform, as it takes longer and has to be performed by two teams. Raising the scrotal flap to contain the spermatic cord and the attached testicle is a method that has been used for reconstructing a penis.[8] In our patient, we used the distally based rectus abdominis myocutaneous flap for reconstructing both the urethra and penis in a one-stage procedure.

There are many procedures for reconstructing the urethra, with the literature citing various advantages and disadvantages for each. Because our patient's father had no significant hair in the abdominal area, we anticipated that the child would probably also have little hair. Therefore we used abdominal skin for the urethra reconstruction. However, electrolysis can be done in patients in advance if there is hair growth.

Six months' follow-up showed no significant atrophy and the flap remained firm. Cosmetically the size is not correct for his age, but this will become less of a problem when he reaches adulthood. There is no sensation with such flaps, which is a problem with all methods, but we hope that progress will eventually yield a solution for this.

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Case Reports

KOHL CONTAMINATION OF THE UMBILICUS CAUSING X-RAY OPACITY: A CASE REPORT

Mukesh Gupta, MD; Shahzad S. Khan, MD

Kohl has been used as an eye cosmetic and eye medication since ancient times. The way in which it is prepared varies from place to place and country to country. Microbial contamination of the eye[1-3] from the use of kohl has been reported by Tabbara and Burd.[1] In addition to its use in the eye, it is also used as paste (in combination with other solvents) applied over the scalp, chest, and abdomen (in and around the umbilicus) of newborns in this part of Saudi Arabia. We encountered an infant who presented with symptoms that were eventually traced to the use of kohl in the umbilical area.

Case Report

A 2-month-old male infant was seen in the pediatric clinic because of excessive crying regardless of the time of day, feeding, posture, and handling that had been present since birth. There was no associated fever, loose bowel movements, constipation, vomiting, or a fall.

The infant weighed 6.5 kg, and all vital signs were within normal limits. There was no evidence of congenital malformations, and detailed examination, including ear, nose and throat, and rectal, revealed no abnormalities. The abdomen was soft. The child had been circumcised a few days earlier and the wound was healing properly. Stool, urine, and the chest x-ray studies were all normal. Plain x-ray film of the abdomen revealed a semilunar radioopaque shadow in the hypogastrium. The child cried during micturation, according to the mother.

A urologist was consulted and the following diagnoses were considered: congenital urogenital tract malformation, calcified foreign body in the bowel, or calcification in the soft tissues or in the bladder.

Foreign body in the gut was ruled out as the child was exclusively breastfed. Calcification in the bladder was also ruled out because the defect shown by the plain x-ray was somewhat higher up than the normal site of the bladder. Intravenous pyelography was planned to assess for the possibility of a congenital malformation of the urinary tract.

While preparing the child for the pyelography, one of the authors noticed some ashen black, hardened matter adherent to the inner fold of the umbilicus. It was removed in pieces by forceps. Pyelography was withheld and a plain x-ray study of the abdomen repeated. The radiopaque shadow was no longer visible on the new film. The foreign bodies which had been removed from the umbilicus were placed at the child's side and another film taken. This film produced a radiopaque shadow similar to that seen on the first film.

The mother admitted that she had applied kohl with some powder in the form of paste over the scalp and abdomen during the neonatal period. No further investigation was done and the patient responded to symptomatic treatment.

Discussion

Kohl is commonly applied to the eyes for cosmetic reasons and is also used for medicinal purposes. Kohl can be contaminated by many organisms[1-3] and can cause complications such as eye infections and abrasions. Our patient manifested a pseudo-clinical complication following its application as a paste applied around the umbilicus. It is a local belief that this will strengthen the abdominal wall there by prevent-

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ing umbilical hernia. Similarly, it is applied over the scalp in the belief that it will promote good and early closure of the anterior fontanelle (Figure 1).

It is highly advisable, especially in infants in this part of the country, to do a thorough examination for the presence of kohl anywhere in the body before doing any x-ray studies.

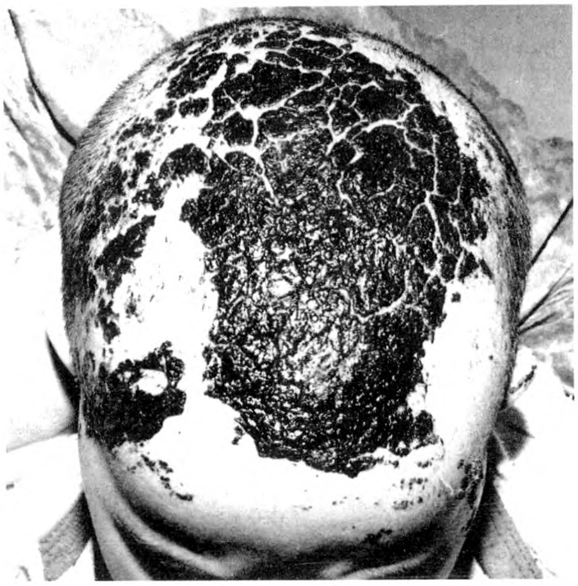

FIGURE 1. Photograph of infant with kohl applied to the scalp in the belief that this will promote early closure of the anterior fontanelle.

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Editor's Note: "First examine the patient."

TRANSFUSION MALARIA IN NEWBORN INFANTS: REPORT OF TWO CASES

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Frequent blood transfusions during intensive care can expose newborns to transfusion-acquired malaria. Asymptomatic blood donors are often the source of the disease.[1] We report two cases of transfusion malaria in newborn infants that were caused by *Plasmodium falciparum,* and encourage heightened awareness of this condition in the sick baby receiving intensive care. Only 18 cases of *Falciparum* malaria in newborns have been reported so far[2] and none appear to have originated from Saudi Arabia or the Middle East.

Case Reports

A male Saudi infant, born at 28 weeks gestation, began to suffer recurrent episodes of apnea when he was 47 days old. He had been ventilated at birth until the age of six days because of respiratory distress syndrome. An episode of submandibular cellulitis at age of 35 days had been treated with antibiotics, with prompt response. He had received three blood transfusions for treatment of anemia and replacement of blood removed for laboratory tests. The blood transfused was less than five days old and had been tested for syphilis, hepatitis B, and human immunodeficiency virus, as per the standard protocol of the blood transfusion department.

On examination the patient was noted to be lethargic, with temperature, 36.9°C, and pulse, 140 beats per minute. The anterior fontanelle felt normal. Findings from systemic examination were normal. Results of complete blood counts (CBC) at this time are given in Table 1. The cerebrospinal fluid (CSF) was clear with 10 white blood cells per mm^3 (normal, 0–25 per mm^3) of which 90% were lymphocytes. The protein concentration in CSF was 0.8 gm/L (normal, 0.5 to 1.3 gm/L) and glucose, 2.5 mmol/L, with a blood glucose level of 6.9 mmol/L (normal CSF to blood ratio, 0.55–1.05). CSF was negative for bacteria and blood cultures were negative.

Ultrasound examination of the brain showed hyperechoic shadowing of the lateral ventricular walls (Figure 1). Coagulation profile and liver function tests, including serum bilirubin (total and direct), total proteins and albumin, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, and alkaline phosphatase, were normal.

Septicemia was considered the diagnosis and he was treated with ceftriaxone and gentamicin. He continued to require ventilation because of recurrent apnea. At the age of 50 days his liver and spleen became palpable at 3 cm and 2.5 cm, respectively, below the costal margin. Blood counts at this time showed pancytopenia (see Table 1). Peripheral smear showed evidence of *falciparum* malaria with intense parasitemia. He was given oral doses of chloroquine (5 mg/kg of body weight stat) followed 6 hours later by 2.5 mg/kg then 2.5 mg/kg once daily for three days. A packed red cell transfusion was given to correct the anemia. The episodes of apnea subsided and he was extubated three days after conclusion of the chloroquine therapy. Repeat CBC showed resolution of the pancytopenia and ultrasound

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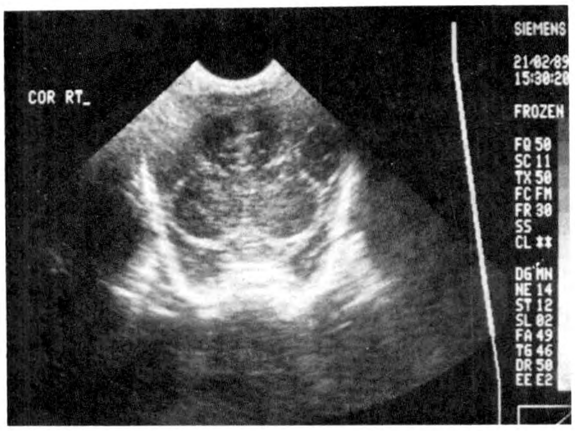

FIGURE 1. Patient 2. Cerebral ultrasound scan of brain showing hyperechoic shadowing of ventricular walls.

TABLE 1. *Complete blood counts.*

	Patient 1		Patient 2	
Blood count	Day 1 of illness	Day 4 of illness	Day 1 of illness	Day 5 of illness
Hemoglobin (gm/L)	125	100	106	96
WBC (10^9/L)	7.8	4.7	15.0	35.1
Differential				
Polymorphs	0.11	0.07	0.27	0.20
Band cells	0.01	0.03	0.1	0.1
Lymphocytes	0.63	0.65	0.54	0.61
Monocytes	0.05	0.12	0.08	0.07
Eosinophils	0.20	0.13	0.01	0.02
Platelets (10^9/L)	284	21	600	60
Reticulocytes	7.9	8.0	3.0	9.0

WBC = white blood cells.

examination of the brain showed disappearance of the hyperechoic shadowing.

The mother of the infant was from Riyadh, which is not an endemic region for malaria. She had no previous history of malaria and her blood smear showed no parasites. The patient was discharged home and remained well at follow-up six weeks later.

Patient 2

A full-term Saudi female infant with epidermolysis bullosa developed fever of 38.9°C at age of 61 days while in hospital. She had received fresh frozen plasma on three occasions and blood transfusion once prior to this. The blood used was less than five days old and fully disease tested, per existing protocol of the blood transfusion department.

Physical examination showed skin changes typical of epidermolysis bullosa, but the infant was otherwise normal. CBC results are given in Table 1. CSF examination and ultrasound scan of the brain revealed no abnormality. She was managed as a case of septicemia with broad-spectrum antibiotics, but fever of up to 39°C continued. At the age of 65 days her liver and spleen became palpable at 3.5 cm and 2.5 cm, respectively, below the costal margin. Repeat CBC showed leukocytosis, anemia, and thrombocytopenia (see Table 1). Blood smear revealed heavy parasitemia with *Plasmodium falciparum*. She was given chloroquine (5 mg/kg orally daily) for five days. Anemia was corrected by packed red cell transfusion. She became afebrile after two days, and clinical and laboratory abnormalities returned to normal in 6 days. The mother was from Riyadh and gave no history of malaria; her blood smear was also negative for malarial parasites.

We were able to trace the blood transfusion for both babies to the same donor who came from Sudan, where *falciparum* malaria is endemic. However, the donor's past medical history, including history of malaria as well as physical examination findings, was negative at the time of blood donation. Blood smear examination and serological tests for malaria are not routinely done in testing of donor blood. A specimen of the donor's blood, retained in the blood bank, was negative for the malarial parasite. Further evaluation was not possible because the donor could not be traced and serological tests for malaria were not available locally.

Discussion

Several factors affect the acquisition of malaria through blood transfusion.[1] Depending on the species, the parasite may persist in asymptomatic carriers from one to over 50 years. Such carriers cannot be detected by routine examination of peripheral smear due to the low degree of parasitemia. Antibody techniques such as agar gel diffusion, passive agglutination, immunofluorescence, and enzyme-linked immunosorbent assay are highly sensitive in the diagnosis of asymptomatic cases of malaria[3] but are not available universally. Although most cases appear following the transfusion of blood stored for less than five days, cases of *P. falciparum* and *P. malariae* have been reported to occur following transfusion of blood stored for 12 to 14 days.[1] The incubation period varies with the species and ranges from a minimum of four days for *P. falciparum* to as long as 80 days for *P. malariae.*[1] The minimum infective dose can be as few as ten parasites.[4]

The malaria in both babies was caused by the same species of *Plasmodium*. Congenital malaria is unlikely since the mothers came from a region not endemic for malaria, had no history of exposure to malaria, and had negative blood smears for malarial parasite. In addition, the age at onset in Patient 2 (61 days) was beyond that described for most cases of congenital malaria, which is usually between three to eight weeks after birth.[5] Both babies had received two-day-old blood from a single donor from Sudan, a country where *falciparum* malaria is endemic. Absent signs and symptoms as well as a negative blood smear do not exclude the carrier state in a person from endemic areas.[1] Although antibody tests were not performed on the donor's blood, there is strong circumstantial evidence linking the occurrence of *falciparum* malaria in both infants and transfusion of blood from the same donor, particularly since the mothers could not have been the source of malaria and since Patient 2 received blood only from this donor.

The diagnosis of malaria was not obvious initially in either patient. The presenting symptoms (i.e., apnea and fever) led to a search for bacterial sepsis. Anemia and thrombocytopenia with leukopenia (Patient 1) and leukocytosis (Patient 2) are typical features of septicemia in neonates. Other findings in our patients and those described in literature[2] (Table 2) are more suggestive of systemic bacterial infection than of malaria.

The significance of hyperechoic ventricular walls in Patient 1 is unknown. It was present during the acute illness and subsided after antimalarial treatment. It may represent cerebral involvement in malaria.

The nonspecific nature of neonatal malaria makes early diagnosis dependent on heightened awareness to the possibility of malarial infection in any sick newborn who has received blood transfusion. Chloroquine is the drug of choice for sensitive strains.[2] The parenteral route is used in very ill children, but vital signs, especially blood pressure, must be closely monitored in these children.[6] Orally administered chloroquine (5 mg/kg/day for five consecutive days) has been used successfully to treat malaria in the neonate,[7] and is safer than parenteral preparations. Based on published information, we prefer the above regimen, which is effective and well tolerated, and is less toxic than parenteral therapy. Quinine and pyrimethamine have been used in resistant cases.[2]

TABLE 2. *Neonatal malaria: clinical profile and laboratory parameters.*

	Thapa et al[2] (%)	Patient 1	Patient 2
Anemia	100	+	+
Fever	90.3	−	+
Splenomegaly	83.9	+	+
Hepatomegaly	64.5	+	+
Raised SGOT/SGPT	57.1	−	−
Jaundice	23.5	−	−
Reticulocytosis	19.3	+	+
Thrombocytopenia	19.3	+	+
Seizures	10.0	−	−
Diarrhea	7.3	−	−
Renal failure	3.2	−	−
Hyperechoic ventricular walls	not done	+	−

SGOT = serum glutamic oxaloacetic transaminase;
SGPT = serum glutamic pyruvic transaminase.

Indepth history taking, direct microscopical analysis of donor blood, and various immunological tests are suitable for screening transfusion malaria in nonendemic regions.[1] Blood smear examination is the least reliable method in asymptomatic carriers because of the diminished parasitemia.

Detailed history taking and exclusion of those who have recently suffered from active disease is the most practical measure. Currently there are no internationally accepted rules for donor exclusion. Criteria vary among countries and are determined by the demand for blood vis-a-vis the local risk of transfusion malaria.[1] Malarial antibody detection tests such as immunofluorescence and enzyme-linked immunosorbent assay are sensitive and specific[3] but until they are available universally, detailed history taking and exclusion of donors who have recently suffered from active disease will remain the most effective and practical measures for screening donors.

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NOSE AND THROAT LEECH INFESTATION: A REPORT OF SIX CASES FROM JORDAN

M. T. Damati, FRCS; M. N. Abo-Shehada, PhD

Leeches inhabit land or fresh water sources (e.g., springs) on which a whole village may depend for their water and may frequently be used by roaming Bedouins and their animals. The hirudinean leeches are occasional parasites of humans and animals, mainly those who come in contact with infested water. They feed on the blood of various hosts to whom they attach themselves and drop off after becoming engorged. Inside the host they may inhabit the upper respiratory tract[1-3] and cause a variety of symptoms, mainly epistaxis, bleeding from the mouth, nasal obstruction, foreign body sensation, stridor, dyspnea, and dysphagia, sometimes ending in death.[4]

We report six cases of leech infestations of the upper respiratory and digestive tract from Jordan.

Patients and Methods

Six patients with leech infestation were seen at the E.N.T. Clinics of H.R.H. Princess Basma Hospital and Jordan University of Science and Technology Health Center during 1987 to 1988. Case histories are summarized in Table 1. The recovered parasites were prepared for identification according to the method of Beaver et al[5] and fixed in formalin.

Results

All six patients complained of bleeding (either from the mouth and/or nose), pallor, or cyanosis. Examination revealed the presence of worms, and patient summaries are given in Table 1.

Case Reports

Patient 1

Direct laryngoscopy in this 50-year-old man revealed congestion of the pharyngeal mucosa caused by the traumatic interference of the patient and his family, edema of the vocal cords, and the presence of a fleshy leech on the right vocal cord that was removed without anesthesia. The patient comes from the southern city of Karak, where he and his family depend on an old well for their water.

Patient 2

This 10-year-old boy had been seen by many physicians and undergone many examinations, including chest x-ray study and rhinoscopy, which were both normal. His hemoglobin was 50 gm/L and he had eosinophilia of 10%. The patient was treated with 5% argyrol ephedrine nasal drops. When the patient sneezed at home, a fleshy leech came out of his nostrils. The patient's general condition subsequently improved and his hemoglobin level rose to 100 gm/L within 2 weeks. The patient lives in the northern city of Ramtha where his family depends on a local spring for their water.

Patient 3

Throat examination in this 35-year-old man revealed the presence of a fleshy mobile mass that when removed under local anesthesia (5% lidocaine spray) proved to be a live leech. The patient comes from Mafraq.

Patient 4

A 50-year-old anxious woman was seen because of painless epistaxis and bleeding from the mouth.

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TABLE 1. *Summary of 6 cases of leech infestations in the upper respiratory digestive tract.*

Patient No.	Age (yr)	Sex	Residence	Location of leech	Hb level (gm/L)	E (%)	Symptoms
1	50	M	Karak	Vocal cord	100	10	Inspiratory stridor, bleeding from mouth, mild cyanosis
2	10	M	Ramtha	Nasal cavity	50	10	Severe recurrent epistaxis, pallor
3	35	M	Mafraq	Pharynx	110	N/D	Severe epistaxis, bleeding from mouth
4	50	F	Irbid	Beneath soft palate	90	8	Painless epistaxis, mouth bleeding
5	40	M	Ghour	Posterior pharyngeal wall	N/D	9	Foreign body sensation, bleeding
6	25	F	Irbid	Base of tongue	80	6	Foreign body sensation, bleeding

M = male; F = female; E = eosinophilia; N/D = not done.

Anterior rhinoscopy revealed the presence of a leech, which was mobile and changeable in size, located beneath the soft palate. The leech was removed without the use of anesthesia. The woman lives in the northern city of Irbid.

Patient 5

This 40-year-old man was seen because of bleeding from the mouth, foreign body sensation, and mild dysphagia. Examination revealed a pale mucous membrane and bleeding from the posterior pharyngeal wall. Lidocaine was applied as a spray to the area followed by suction clearance, and a fleshy mass was removed from the posterior pharyngeal wall using Luc's forceps. The patient lives in the Ghour area.

Patient 6

A 25-year-old woman from Irbid complained of foreign body sensation in the mouth and glossodynia, with bleeding from the throat. Indirect laryngoscopy after application of anesthetic spray (5% lidocaine) revealed a fleshy mass at the base of the tongue. The leech was removed with the help of Luc's forceps.

The formalin-fixed specimens of the leeches were gray with no definite markings, measuring 3 to 5 cm in length and 1 to 1.5 cm in width. There were no auricles on the posterior segments and no teeth, but five pairs of eyes were present in the anterior segments. These specimens were identified as hirudinean leeches according to the description of Beaver et al.[5] All patients were exposed to water sources that contained aquatic leeches.

Discussion

This report describes cases of hirudinean leech infestation in inhabitants of Jordan, an observation reported from other neighboring countries such as Saudi Arabia[6] and Iraq.[7]

Diagnosing leech infestation in the upper respiratory passages is difficult and many cases are not detected at the first examination. Sometimes the parasite is in a hidden place in the throat, especially the postnasal space, vallecula, and hypopharynx. Suction clearance of the blood from the throat and nose and good lighting of the area are indispensable for better inspection. Following the application of local anesthetic spray (5% lidocaine), the leech shrinks and becomes detached from the attachment site within 2 minutes. Thus the use of a local anesthetic agent may help detach the parasite passively, thereby avoiding excessive damage to the tissue and hence the danger of granuloma formation at the attachment site.[6]

All patients had iron deficiency anemia, with low hemoglobin levels. Patient 2's level reached 50 gm/L, and two weeks following removal of the parasite, the level rose to 100 gm/L.

Eosinophilia was found in five of the patients. This is observed with many parasitic infections[8] and may be used in the differential diagnosis of other nose and mouth bleeding disorders.

Respiratory and digestive tract leech infestation should be considered whenever patients present with epistaxis or bleeding from the mouth and a history of recent contact with fresh water sources.[9] Further study of the prevalence of hirudinean leeches in fresh water sources in Jordan may identify infested water sources and help in the control of the parasite.

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A FATAL CASE OF ASPIRIN IDIOSYNCRASY

Suliman Alballa, FRCP(C)

Aspirin is probably the most widely prescribed drug in the world and is present in over four hundred proprietary drugs. It is not an absolutely safe drug and should be taken only for appropriate indications.[1] Many side effects have been ascribed to aspirin, probably caused by different mechanisms and with variable incidences. The respiratory side effect is considered an idiosyncratic reaction.[2] This term refers to a qualitatively abnormal reaction to a drug that is not due to an allergic mechanism.[2] Idiosyncratic reactions are serious but underdiagnosed,[3] and their relationship to aspirin intake may be overlooked if proprietary drugs containing aspirin are used.

Case Report

A 50-year-old Saudi man was admitted to the hospital following a 5-day history of shortness of breath and wheezing. He had had no history of allergy or atopy, but did describe recurrent episodes of nasal discharge, and bronchial asthma had been diagnosed when he was 33 years old. He was not on treatment at the time of admission.

Examination revealed bilateral expiratory rhonchi. He also had a nasal polyp on the right side. He was treated with a salbutamol inhaler and intravenously administered aminophylline and was discharged five days later on oral aminophylline. On the day of discharge, when at home, he took two acetylsalicylic acid tablets (aspirin) for headache. A few minutes later he collapsed and was brought to the hospital in a state of respiratory arrest. He was successfully resuscitated and was discharged with the diagnosis of aspirin idiosyncrasy and aspirin-induced asthma. Both the patient and his family were informed about this idiosyncrasy and he was instructed to avoid any aspirin-containing products.

Seven months later, he was seen by his general practitioner for a cold and was given Otrivin (xylometazoline hydrochloride) and Sedergine (330 mg of aspirin, 200 mg of ascorbic acid). Within minutes of taking the first dose he collapsed and was brought to the hospital, where on arrival, he was found to be in cardiopulmonary arrest. He was resuscitated and transferred to the intensive care unit. Unfortunately, he remained comatose and brain death was diagnosed.

Discussion

Aspirin is one of the most widely used drugs in medicine. Since it was first marketed by the Bayer Company in 1899, many side effects have been reported. Gastrointestinal side effects, especially bleeding, are the most common. The first death attributed to aspirin was reported from Germany in 1902.[2] Soon after, aspirin-induced asthma was reported. Somter and Beers[4] in 1967 reported a triad of nonallergic rhinitis, nasal polyposis, and bronchial asthma that was associated with aspirin ingestion. It was later found that aspirin-induced idiosyncratic reactions may occur without nasal polyps in approximately 30% of patients.[5] Respiratory side effects related to aspirin use are common, but are underdiagnosed.[3] The frequency varies considerably according to the patients surveyed and to the criteria used in their selection, and range from as low as 0.9% of normal persons to 2.4% of asthmatic patients, based on history only.[6] This contrasts with the results of studies using an oral aspirin challenge in which 20 to 34% of asthmatic patients exhibited aspirin-induced asthma.[3,7] The incidence was much higher if patients with a positive history of aspirin-

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induced asthma were included.[7] It was also found that the response to aspirin challenge may change from one occasion to the other.[8] The problem of aspirin idiosyncrasy is compounded by the finding that many other substances, including other nonsteroidal antiinflammatory drugs,[9] tartrazine,[7,9] and sulfinpyrazone,[2] are highly cross reactive in aspirin-sensitive asthmatics during aspirin challenge.

The pathogenesis of aspirin-induced asthma is not clear. Various theories have been suggested but none explain all aspects of the syndrome. Immunological mechanisms are unlikely to be a major factor. Among the facts discounting an immunological mechanism is that sensitivity cannot be passively transferred. Also, studies on both lymphocyte transformation and skin testing have been negative.[2] In addition, the difference in the chemical structures of drugs producing clinical symptoms makes immunological cross reactivity unlikely. The role of complement activation has recently been challenged with the finding of normal complement levels in aspirin-sensitive asthmatics during aspirin challenge.[10]

The prostaglandin hypothesis[9] suggests that aspirin idiosyncrasy may be mediated by changes in the production of prostaglandin. Cyclooxygenase inhibition by aspirin and other nonsteroidal antiinflammatory drugs (NSAID) would lead to a decrease in prostaglandin E_1 (PGE_1). PGE_1 is both a bronchodilator and inhibitor of histamine release from basophil and mast cells in the lung. This inhibition is augmented by a shift of prostaglandin synthesis to the lipoxygenase pathway, with the production of leukotrienes and increased bronchoconstriction.

More recently, in vitro studies of platelets from patients with aspirin-induced asthma revealed generation of a cytocidal supernatant and a burst of chemiluminescence following exposure to aspirin and other NSAID. These abnormalities were not seen in platelets from controls and from aspirin-sensitive asthmatics who had undergone aspirin desensitization. These findings suggest platelets have a role in the pathogenesis of aspirin-induced asthma and may also be of diagnostic value.[11]

Aspirin idiosyncrasy should be suspected in any patient with bronchial asthma. Aspirin and other cross-reactive drugs should be avoided in such patients even if they have no history of aspirin idiosyncrasy, as only a small proportion of idiosyncratic patients report a positive history.[2,3] Aspirin challenge is not recommended to prove the diagnosis of aspirin idiosyncrasy, because it may precipitate a serious reaction. Such a procedure, which may rarely be indicated in asthmatic patients with other concomitant diseases such as rheumatoid arthritis, should be conducted with extreme caution and under strict control.[2,3,9]

Aspirin is present in over four hundred proprietary drugs and serious reactions may be precipitated by their use. To avoid such a catastrophe, the patient should be clearly instructed not to take any aspirin-containing product. The presence of aspirin in many over-the-counter preparations and the need for avoidance of such preparations cannot be overstressed. Also, as an additional safeguard, drugs that contain aspirin should be clearly labeled in that regard. These measures should help to reduce the risk of such a reaction in susceptible patients.

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GASTROINTESINAL PHYTOBEZOAR OBSTRUCTION: REPORT OF THREE CASES

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Small bowel and gastric outlet obstruction due to phytobezoars remain rare following gastric operations, but they are an interesting clinical entity. The origin of the word is contested; some claim that it comes from the Arabic "bad zehr," others from the Persian "pad zahr," and still others from Turkish "pan zehir," all meaning "anti-poison."[1,2] In bygone times, bezoars from goats and antelopes were ground and ingested for their supposed curative properties and as antidotes to poisons. Three types were recognized according to their composition: trichobezoar (hair), phytobezoar (fruit and vegetable fibers), and trichophytobezoar (a mixture of the two). We will discuss the pathogenesis, diagnosis, and management of three such cases encountered in our practice.

Case Reports

Patient 1

A 53-year-old man was seen because of colicky abdominal pain, vomiting, and absolute constipation of 3 days' duration. He had had an appendectomy in 1952 and in 1977 a truncal vagotomy and drainage procedure for chronic duodenal ulcer. At admission he was noted to be moderately dehydrated and was found to have bad teeth and poor mouth hygiene. His abdomen was distended and bowel sounds were increased. X-ray study of the abdomen showed multiple fluid levels. Apart from a plasma urea level of 21 mmol/L, all routine investigations were normal. Adhesive intestinal obstruction was diagnosed, but the patient did not respond to conservative management that consisted of intravenous fluid therapy, nasogastric decompression, and clinical and abdominal x-ray follow-up.

A doughy mass, about 8 cm in length, was found to obstruct the ileum approximately 60 cm from the ileocecal junction. The proximal bowel was dilated. The drainage procedure consisted of antecolic gastrojejunostomy. No similar obstructing masses were found in the small intestine. The mass was easily milked into the cecum and along the ascending colon. Postoperatively the patient made an uneventful recovery. He was discharged well and advised to attend to his teeth, masticate food thoroughly, and avoid orange pith or seeds of other fruits.

Patient 2

A 50-year-old man was seen by us because of colicky abdominal pain, repeated vomiting, and absolute constipation. Five months earlier he had been admitted to another hospital because of vomiting and dysphagia. At that time, upper gastrointestinal endoscopy revealed a bolus obstructing the cardia and a segment of the pyloroduodenal canal. An attempt at endoscopic disimpaction failed and the boluses were removed surgically.

In 1965 the patient underwent a truncal vagotomy and pyloroplasty for chronic duodenal ulcer. This new attack was precipitated by a heavy meal of various constituents including vegetables, but no orange pith. Clinically he was dehydrated, had tachycardia, and a distended abdomen with increased bowel sounds. X-ray study of the abdomen showed multiple fluid levels. The results of other investigations were normal except for a plasma urea level of 16 mmol/L. After initial resuscitation the patient underwent exploratory

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laparotomy and was found to have a 10-cm long mass that obstructed the small intestine approximately 100 cm from the ileocecal junction. The bowel was dilated proximal to this obstructing mass and two small masses could be felt intraluminally. The rest of the small intestine and stomach was normal. The mass was milked to the cecum and then to the ascending colon. He made a smooth recovery and was discharged with advice about diet and mastication.

Patient 3

A 38-year-old man who had had a truncal vagotomy and antrectomy 2.5 years previously for prepyloric and duodenal ulcers was seen because of upper abdominal pain, a feeling of fullness, and intermittent vomiting for the previous seven days. Clinical examination disclosed fullness in the upper abdomen; positive succession splash, and normal bowel sounds. Plain x-ray study of the abdomen revealed a distended stomach filled with food particles. A wide-bore nasogastric tube was inserted and disimpaction successfully achieved with repeated gastric irrigation and suction. However, after removal of the tube two days later, the patient could not tolerate fluid and started to vomit. A barium meal revealed a filling defect near the gastroduodenal anastomosis with run-off of the dye to the duodenum (Figure 1). Intravenous hyperalimentation was started and the abdomen was surgically explored. A tightly packed mass of food particles, about 8 × 8 cm, was removed from the stomach. The gastroduodenal anastomosis was found to admit two fingers; however, a wider gastrojejunal anastomosis was established anterior to the colon. The patient recovered and remained fit and well during 1.5 years of follow-up.

Discussion

The initial case of phytobezoar–small bowel obstruction following gastrectomy for duodenal ulcer was described by Seifer.[3] Between 1955 and 1972, over 150 cases of phytobezoar obstruction of the gastrointestinal tract were reported.[4] Moseley[5] (in 1967) was the first to record a case of gastric outlet obstruction due to phytobezoar following vagotomy and pyloroplasty. In 1973 Mir and Mir[6] described phytobezoar–small bowel obstruction following vagotomy and gastrojejunostomy. In most cases orange pulp was the cause of the obstruction; however, various other foodstuffs such as figs, apples, grapes, persimmons, coconuts, cabbage, beans, and potatoes were implicated.

The interval from surgery to the development of symptoms of phytobezoar is variable, and has been observed to range from a few months to thirty years. In our cases, obstruction developed in one patient 10 years after vagotomy and drainage, in the second 22 years after vagotomy and drainage, and in the third 2.5 years after vagotomy and antrectomy. One report cited phytobezoar–small bowel obstruction as accounting for 2.9% of the cases of total small bowel obstruction that involve surgery.[7] In our hospital, from 1983 to 1987, 61 patients had laparotomy for small bowel obstruction; two had phytobezoar obstruction, yielding an overall incidence of 3%.

The rapid gastric emptying following gastrectomy probably accounts for why most of the bezoars are found in the small bowel after such a procedure. Pylorus control of gastric emptying is removed in gastrectomy, destroyed in pyloroplasty, or bypassed in gastrojejunostomy. The antral mill is grossly interfered with by antrectomy or vagotomy. Abolition of this mill means that larger food particles and undigested fruit and vegetable fibers are deposited directly into the small bowel and thereby form the nidus for the development of phytobezoar.[8]

In our patients, phytobezoar intestinal obstruction occurred after vagotomy and drainage, and this finding has also been reported elsewhere.[6,7]

The site of the bezoar is usually suggested by the clinical picture. Gastric phytobezoar may be suggested by burning epigastric pain, nausea, vomiting, weight loss, early satiety, and postcibal fullness or gastric outlet obstruction. The diagnosis is clinched either by endoscopy or barium meal. Treatment is nonsurgical: gastric lavage, proteolytic enzymes, with or without endoscopic removal, and clear fluid diet have been found to be successful in dealing with gastric bezoar.[9,10] Prolonged enzymatic activity or energetic mechanical treatment may lead to ulceration, perforation, obstruction, or gastritis.[9] Gastrostomy and surgical removal are required if these conservative methods fail, as is in our Patient 3.

Small bowel bezoar presents with classic features of acute small bowel obstruction. At laparotomy, milking the mass to the large bowel is usually enough, and only when this is impossible should enterotomy be employed. The entire gastrointestinal tract must be examined carefully for the presence of other bezoars, to avert any need for further surgical intervention.[2]

Phytobezoar tends to recur in up to 33% of cases;[10,11] it is therefore imperative for the clinician to instruct patients about suitable diets and the need for adequate mastication of raw fruits and vegetables containing fibers. This is even more important for patients who have undergone operations destroying the pyloric mill. Drugs that stimulate motility (e.g., metoclopramide) may be added to reduce the possibility of recurrence.[12]

Highly selective vagotomy seems, so far, to be devoid of the complication of phytobezoars developing in their wake, lending further credence to the theory of pyloric mill loss as the source of the problem, which in this operation is preserved.[7]

Acknowledgments

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Letters to the Editor

The *Annals of Saudi Medicine* welcomes letters to the Editor from its readers. They may be on any topic, though the Editor especially encourages discussion of papers published in the *Annals*. Letters should be no more than 100 typewritten lines in length, typed double-spaced, and submitted in triplicate. Letters may include one figure or brief table and up to five references. Submission of a letter constitutes permission for the *Annals* to use it for publication. Letters should not duplicate similar material being submitted or published elsewhere, and the *Annals* reserves the right to edit letters submitted. Letters referring to a recent *Annals* article should be received within 6 weeks of the article's publication.

Renal Histology in Saudi Population with Overt Nephrotic Syndrome

To the Editor: We read with interest the paper of Akhtar et al[1] and would like to comment on our own experience with renal pathology in Saudi Arabia, specifically our findings in Saudi patients who underwent renal biopsy for overt nephrotic syndrome up to June 1987. Whenever possible, specimens were assessed by light microscopy, immunofluorescence, and electron microscopy.

Renal biopies were performed in 84 adults (mean age, 29.3 years; range, 17–75 years) and 44 children (mean age, 7 years; range, 1–15 years), all with overt nephrotic syndrome. Secondary cases of glomerulonephritis were excluded from this study. Only children who were either steroid dependent or nonresponsive underwent biopsy. The histological results are shown in Table 1.

In our series the incidence of focal segmental glomerulosclerosis and mesangial proliferative glomerulonephritis in adults was less than that reported by Akhtar et al, whereas the incidences of minimal change disease and mesangiocapillary (membranoproliferative) glomerulonephritis were higher. Moreover, in the pediatric population, the incidence of minimal change disease and focal segmental glomerulosclerosis in our series was the reverse of that reported by Akhtar et al.

TABLE 1. *Summary of histological findings.*

Disorder	Children (N = 44) (%)	Adults (N = 84) (%)
MCD	40.90	13.1
MPGN	11.4	8.3
FSGS	11.4	15.5
MCGN	6.8	25
MGN	2.3	14.3
DPGN	25	17.8
Others	2.3	5.9

MCD = minimal change disease; MPGN = mesangial proliferative glomerulonephritis; FSGS = focal segmental glomerulosclerosis; MCGN = mesangiocapillary (membranoproliferative) glomerulonephritis; MGN = membranous glomerulonephritis; DPGN = diffuse proliferative glomerulonephritis.

One explanation for why our results differ from those described by Akhtar et al is that our patients were selected only if they presented with signs and symptoms of overt nephrotic syndrome and do not include those who presented with other indications for renal biopsy. In the study of Akhtar et al, the indications, although not specified, probably included all indications for renal biopsy. Moreover, for the pediatric subgroup, inclusion in our series was determined by the presence of nephrotic syndrome and either the lack of response to steroids or dependency on steroids. This explains the relatively small percentage of minimal change disease and relatively large incidence of proliferative glomerulonephritis. The discrepancy between our results and those of Akhtar et al indicates the need for more data in this field and suggests the need for a register for cases of glomerulonephritis in the Kingdom of Saudi Arabia, under the auspices of the National Kidney Foundation.

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Editor's Note: The preceding letter from Drs. Al-Khader, Al-Sulaiman, and Dhar summarizes the renal biopsy experience in the Department of Nephrology at the Armed Forces Hospital in Riyadh. As noted by these authors, the difference in the apparent incidence of morphologic types of glomerulonephritis between Al-Khader's group and those published by Akhtar et al earlier this year is probably due to different criteria used for the selection of renal biopsies. Al-Khader's material was selected on the basis of clinical presentation with overt nephrotic syndrome, whereas the King Faisal Specialist Hospital material was from an unselected series of renal biopsies.

Drug Resistance in Tuberculosis

To the Editor: We recently reported the prevalence of resistance to antituberculous drugs observed in affected patients living in Riyadh.[1] Resistance to one or more drugs was found in 92 (21.3%) of 432 patients with culture-proven tuberculosis. Resistance to isoniazid was the most common (19.4%), followed by resistance to rifampicin (9.7%) and streptomycin (5.1%). One aspect that was not documented in our report was the difference in drug resistance between pulmonary and extrapulmonary tuberculosis. Of all our patients, 87 had extrapulmonary disease, and this included tuberculous lymphadenitis, meningitis, peritonitis, and abscess as well as renal, bone, and joint tuberculosis. None of these patients had had previous antituberculosis therapy. The rate of resistance to antituberculous drugs among these patients was 10.3%. Resistance to isoniazid was found in 9.2% and to rifampicin in 3.4% of patients. Table 1 shows a comparison of resistance between pulmonary and extrapulmonary isolates. The rate of resistance to antituberculous drugs was higher among patients with pulmonary disease. This may be explained by the fact that a large proportion of patients with pulmonary disease (27%) had had previous antituberculous therapy. In addition, pulmonary lesions have a larger bacterial population than do extrapulmonary sites. Drug resistance in mycobacteria occurs as the result of mutant bacilli that arise in the lesion even before therapy.[2] The larger the bacterial population, the more resistant are the mutants. These emerge as resistant organisms when sensitive bacilli are suppressed by drugs.

TABLE 1. *Comparison of resistance between pulmonary and extrapulmonary tuberculosis.*

Patient and resistance	Pulmonary tuberculosis (N = 345)		Extrapulmonary tuberculosis (N = 87)	
	No.	%	No.	%
No. of resistance patients	150	43.5	14	16
Resistance to:				
Isoniazid	76	22	8	9.2
Rifampicin	39	11.3	3	3.4
Streptomycin	20	4.8	2	2.3
Ethambutol	15	3.2	1	1.1

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Symposium Abstracts

SYMPOSIUM ON PRIMARY HEALTH CARE

Sponsored by The Joint Board for Postgraduate Medical Education,
Institute of Public Administration, Riyadh
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TRAINING IN PRIMARY HEALTH CARE, JC Murdoch, Department of General Practice, Medical School, Dunedin, New Zealand

Effective working in the area of primary health care requires from professionals differing emphases and perspectives from those taken by workers in other traditional specialist medical disciplines. This talk examined the geography of primary health care and identified the appropriate knowledge, skills, and attitudes that are required to work in the area. The educational strategies designed to impart these approaches were then discussed, particularly with reference to curriculum design, implementation, and assessment.

QUALITY ASSURANCE IN PRIMARY HEALTH CARE, JC Murdoch, Department of General Practice, Medical School, Dunedin, New Zealand

More and more government agencies are being persuaded to expend a greater proportion of the health care budget in primary health care. Assuring quality in this sector requires full understanding of all aspects of the system and an assessment of quality at each point. In this talk I examined the structure, access, process, and outcomes of primary health care and discuss ways in which quality assurance programs can be designed in such a way as to provide an accurate statement of quality without interfering with the work of the primary health care physician.

PHC ORIENTATION OF HEALTH PROFESSIONALS, YY Al-Mazrou, PSM Rao, General Directorate of Health Centres, Ministry of Health, Riyadh

The need for training the PHC professionals, especially the physicians and nurses, was one of the important recommendations made by the International Conference on PHC at Alma Ata (1978). The emphasis was on social re-orientation, motivation to serve the community, and development of technical skills through exposing them simultaneously to field activities. Accordingly, since the initiation of PHC implementation (1404H), the MOH has undertaken training programs tailored to motivate and orient the PHC teams, improving the skills of different categories of personnel, and quality improvement in individual PHC service components. The author reviewed in detail the content, schedule, and evaluation of such basic category and selective training courses conducted in different regions of the Kingdom and their contribution in establishing a strong PHC base, while projecting the future training needs.

TRAINING PHC MANAGERS TOWARD HFA 2000, PSM Rao, YY Mazrou, SN Shehri, Health Centre Department, Ministry of Health, Riyadh

Strengthening of midlevel primary health care (PHC) management, on which the progress of PHC development depends, is one of the strategic processes adopted by the Ministry of Health (MOH) even from the initial stages of implementation. The PHC managerial process involves a variety of skills related to planning, monitoring, supervision, and evaluation, for which the professionals at these levels had no or minimal exposure during their formal medical education. Hence, the selection of technically qualified supervisors, and motivating them toward the PHC approach and inculcation of skills required, is of prime importance which can only be achieved by exposing them to structured and scheduled inservice training and monitoring their performance through periodic evaluation. This paper outlines the content of the curriculum, the schedule, methodology, and evaluative procedures of such training conducted in different regions of the Kingdom. A review of the training protocol and the experience gained through such eight courses was discussed with suggestions for future protocol amendment.

AN OUTLINE OF THE TRAINING PROGRAM: COLLEGE OF MEDICINE & MEDICAL SCIENCES, ARABIAN GULF UNIVERSITY, BAHRAIN, H Al-Shazali, Community Medicine, College of Medicine and Medical Sciences, Arabian Gulf University, Bahrain

The main objective of medical schools is to train physicians who will upgrade and improve the standard of health services in the community. This can best be achieved by knowing and addressing the health problems in the community *(community oriented)* which in turn can best be achieved by bringing the student and the staff in more physical contact with the community and the community health institutes *(community based)*. With real patient and health problems serving as the core to curriculum, the medical student gains a natural learning stimulus and relevance, the student exercises reasoning ability while gaining new factual knowledge and experience, and on top the student becomes accustomed to learning from patients whom he or she looks after *(problem solving)*. In solving these problems the student depends primarily on his own efforts, utilizing the available resources. This helps to cultivate the habit of individual and continuous learning. As the student learns through problems, the approach has to be integrated, the student becomes familiar with the anatomy, physiology, biochemistry, and clinical aspects as dictated by that particular problem. Therefore, the whole curriculum has to be structured in such a way as to expose the students to the most common problems in the community, utilizing and creating the learning situations that will best provide the needed knowledge and skills. The program in the College of Medicine & Medical Sciences, Arabian Gulf University, has been so designed. It is a six-year program plus a one-year internship. The six years are divided into three phases, premedical, medical phase one, and medical phase two. The learning situations consist of three standards—concepts and principles, professional skills, and community health. Individual disciplines do not have major roles. The learning is mainly conducted in small group tutorials and teaching rounds with no formal lectures. The assessment is formative and summative through continuous evaluation and end-of-year examinations. The program has its problems, especially with implementation, and needs to be continually evaluated and modified. Strictly speaking there is no purely innovative program or purely traditional program; most schools lie in between and adapt to either approach as suits them.

A MODEL TRAINING PROGRAM IN MCH, SN Al-Shehri, M Baldo, Health Centre Department, Ministry of Health, Riyadh

This is a presentation of the Ministry of Health experience in organizing and implementing a model training program for health centre staff (especially doctors and midwives) to upgrade the maternal and child health care services in the Kingdom. Training materials were developed both in Arabic and English. Two training courses have been conducted. Twenty-three physicians and 32 midwives and nurses were trained. Pre and post tests were developed and conducted. Evaluation of the two courses by the trainee and the trainers will be presented, in addition to discussions of the constraints faced during the implementation and recommendations for expansion of such a model training program.

THE MORNING SESSION: A TOOL FOR TEACHING COMPREHENSIVE PRIMARY HEALTH CARE, AZ Taha, A Al-Bar, H Bella, S Assuhaimi, Department of Family and Community Medicine, College of Medicine and Medical Sciences, King Faisal University, Dammam

We describe a new approach to teaching resident physicians comprehensive primary health care. This is one of the activities of a four-year training program of Fellowship in Family and Community Medicine organized by the Department of Family and Community Medicine, King Faisal University, Dammam. The aim is to help residents understand and apply the concepts of comprehensive primary care and have a holistic approach to solving the health and health-related problems of individuals, families, and the community. The morning session with its several components has many benefits, ranging from improving the quality of patient care, management, and administration of primary care services at the health center to identifying strengths and weaknesses of the training program and health care delivery. The format of these sessions included small group discussions, student presentations, independent learning, lecture discussions, and case studies. The sessions were perceived positively by residents. The sessions also provided data for formative and summative evaluation of residents and for constructing learning materials.

A PROPOSAL OF TRAINING PROGRAM OF MOSTAKHDAM WORKING IN PRIMARY HEALTH CARE CENTERS IN SAUDI ARABIA, MH Al-Osimy, King Saud University, College of Applied Medical Sciences, Riyadh

One of the main principles of primary health care (PHC) is that "people have the right and duty to participate individually and collectively in planning and implementation of their health care." This necessitates the propagation of knowledge concerning health among the community. Such objectives cannot be achieved by professionals alone; other nonprofessionals can and should be involved in health education activities. In PHC centers, potentially effective nonprofessionals who understand the life style of the local inhabitants, live within the area served, and who can be utilized for community education are the Mostakhdam. The areas to be considered are: (1) the present situation of Mostakhdam, rationale for training, expected outcome of training; (2) a suggested training program for female Mostakhdam; and (3) preliminary program conducted for female Mostakhdam in PHC centers in Jeddah.

THE EFFECTS OF A TRAINING PROGRAM IN GROWTH MONITORING OF UNDER-5 CHILDREN ON HEALTH PERSONNEL AND MOTHERS IN AL-BAHA, KSA, MS Al-Ghamdi, H Bella, M Salih, Ministry of Health, Dammam

Growth monitoring is recognized as curative as well as preventive in the promotion of child health. This study aimed at evaluating the effectiveness of a pilot training program in growth monitoring. An experimental study was mounted in which problem solving and practical and group discussion methods were used. Pre, post, and follow-up tests were used to evaluate the effectiveness of the training. A review of childrens' charts, indicating the frequency of visits for growth monitoring, was also undertaken as an indicator of effectiveness. The knowledge, attitude, and practice (KAP) of mothers were studied before and after training. The results showed that the KAP of health personnel and mothers has improved significantly. The mean score had improved from 9.7 in the pretest to 16.3 in the post-test, for health personnel. The knowledge of mothers on the growth chart had changed significantly, as had the frequency of their visits. The mean number of visits six months before the training was 1.03 visits, while after six months it was 1.38 visits. The study established the feasibility of training programs in growth monitoring for all categories of health workers. Such programs could be incorporated in casual and continuous medical education curricula for PHC in the Kingdom of Saudi Arabia.

QUALITY ASSURANCE IN PRIMARY CARE: CONCEPTS, PROBLEMS, AND OPPORTUNITIES, A Hutchinson, Health Care Research Unit, University of Newcastle upon Tyne, England

Primary care poses some special problems in the field of quality assurance, as well as some exciting opportunities. Because of the unorganized way in which illnesses present to primary care practitioners and because of the varied organization, from village nurse to a city health centre, it is difficult to describe optimum care. Yet primary care is the point of first contact with the health services for an increasing number of people in an increasing number of countries. It is therefore important to be able to explain what primary care does, how well it is done, and how practitioners may ensure quality service. In this first of two linked papers, there are a number of themes that form the basis for the second, more practical, paper. These themes relate to questions about the nature of quality assurance and performance review—what it is, why it is necessary, and who should do it. Discussion of these themes will lead to the key issues of both papers. First, how to determine the focus of primary care quality assurance—what aspects of care should be examined. Second, the need to set clinical objectives against which to measure performance—what are clinical standards and what do they look like. Third, managing the results of performance review—changing clinical behavior in the light of less than optimum results. One important thread runs through both papers. Quality assurance is often difficult and always challenging. A measured approach is essential.

WHAT SORT OF CONSULTATION? (A STUDY OF THE QUALITY OF PATIENT–DOCTOR ENCOUNTERS IN PRIMARY HEALTH CARE CLINIC), SA Al-Shammari, Department of Family & Community Medicine, College of Medicine, King Saud University, Riyadh

The records of 1222 consultations (patient–doctor encounters) were selected randomly from the files of ten primary health care centers. The quality of consultations, as reflected by the duration of the patient–doctor encounter, and the content of this encounter were studied in 17% of all health centers in urban Riyadh. The data were collected for the entire year using a structured questionnaire/interview form. The mean consultation time was 5.69 minutes ± 4.276 SD. (The mode was 3 minutes.) The following factors were found to increase the mean consultation time: male sex, non-Saudi national, high education of the patient, the professional, and the married patient. Follow-up visits of patients and the doctor's interest in pediatrics led to an increase in the mean consultation time. Elderly patients took more time than younger ones. Elderly doctors spent less time with their patients. Other factors that increased or decreased the mean consultation time were discussed. Due to the pressure of time and more patients waiting to be seen, primary health care doctors resorted to issuing prescriptions more than spending time with the patient. Doctors tended to manage the presenting problems, e.g. sore throat, but would forget or neglect involving the patient in discussion about modifying help seeking behavior or preventive or health promotive activities. 76% of consultations ended in prescriptions. The referral rate was 4% and the investigation rate was 11%. Recommendations for improving the quality of consultation in the primary health care setting were provided.

A STUDY OF THE QUALITY OF REFERRAL LETTERS IN A HEALTH CARE CENTRE IN RIYADH, JS Jarallah, Department of Family and Community Medicine, College of Medicine, King Saud University, Riyadh

This is a study of the quality of 57 referral letters chosen randomly from records at the Darayah Health Centre in Riyadh. During Shawal 1409 there were 221 referrals, representing a 4.3% referral rate at the Centre. The majority of patients were referred to pediatricians (24.6%), obstetricians and gynecologists (21%), dermatologists (12.3%), internists (12.3%), and otolaryngologists (10.5%). The reason for referral was mentioned in 95% of the letters. The majority of patients were referred for general therapeutic advice (35%), routine specialist examination (14%), for more sophisticated tests or procedures (12%), and in 19% of the cases the reasons were vague. The letters were poorly written in 30%, satisfactory in 30%, and good in 40%. The provisional diagnosis was specified in 53 of the referrals with the name of referring physician clearly written in only 35%. Feedback from consultants was poorly written in 47% of the letters, with the name of the consultant clearly written in 59.6%. Final diagnosis was the same as that of the primary care physician in 68% of the cases. Decision on the patient's future care was not specified in more than half of the feedback letters. Recommendation was clearly stated in only 53% of the feedback letters. All these parameters will be compared with a representative sample of referral letters from another health center in Riyadh using a scoring system.

EVALUTION OF EFFICIENCY OF THE REFERRAL SYSTEM IN RURAL PHCC, MR Al-Kashif, Al-Nabaniyya Primary Health Centre, Gassim Health Region, Arras

An obligatory referral system was started in 1.7.1409H in all regions which is considered a natural qualitative development in PHC program implementation: rural centers which are distributed all over Saudi Arabia, constitute about 60 to 70% of PHC centers. This study aims to evaluate the efficiency of the referral system in rural areas. The study was conducted in three centers 80 to 100 km from the nearest general hospital. Data were collected by doctors from 600 patient referral papers of all such cases in the second half of the last year, collected also from registers of referred cases, individual patient's family records, replies from hospitals, and registers of patients with chronic diseases. Data were analyzed according to the patient's personal history, diagnosis of his illness, specialist to whom he was referred, whether he was investigated and received treatment before referral, the different causes, and results of the referral. From this study we can determine the most common reasons for referral and specialties needed to benefit most from this system, which will help in the proper design of training classes and symposia, including common medical problems met by rural doctors and trying to arrange rotational visits by specialists to their related centers.

QUALITY ASSURANCE IN PRIMARY CARE: A PRACTICAL GUIDE, A Hutchinson, Health Care Research Unit, University of Newcastle upon Tyne, England

Few primary care practitioners have experience with quality assurance methods. This is partly because the initial drive has been in high-cost hospital centers, but is also because it is more difficult to do in primary care. Unlike hospitals there is often no discrete intervention that can be seen to have an effect on patient well-being. Much illness encountered in primary care is chronic, care being given sporadically over many years, often with only minor changes in health status. Thus a cautious and careful approach to quality assurance is recommended, starting from small, discrete, and achievable tasks. These allow a sense of success and optimism while contributing to the learning process. Drawing on the concepts expressed in the first paper, the following steps will be considered: (1) choosing a topic for review—what are the options, how are the choices made; (2) clarifying the questions to be asked—what is the nature of the service or problem under review, is it understandable; (3) setting clinical objectives—why are they so important, what do they look like, how should they be set, who should set them; (4) undertaking performance review—setting up a review, collecting and analyzing information; (5) feeding back information to clinicians—how is it done, by whom, and who should have access to it; and (6) using information and managing change—how can clinicians assimilate information and change clinical practice where necessary. Quality assurance is a process of continuous review and change. Exciting opportunities exist for improving clinical practice and patient care.

MANAGEMENT INFORMATION SYSTEM AND MICROCOMPUTER APPLICATIONS IN PRIMARY HEALTH CARE PROGRAMS, HA Hussein, Primary Health Care Department, Madina Directorate of Health Affairs, Madina Munawara

The main constraint reported mostly by all countries is inadequate information support for the managerial process of PHC programs. However, this constraint can be overcome by introducing microcomputers in conjunction with well-designed and targeted MIS that will improve PHC management through timely and informed decision making. The aim of this study is to evaluate the role of MIS and microcomputer applications in PHC programs. Data on immunization (infant aged 0–1 years and women aged 5–45 years), antenatal, natal, and postnatal care activities were collected from PHC centers in the Al-Madina region. The collected data were edited, stored, retrieved, and analyzed using microcomputer and appropriate software. The results were very successful and beneficial in monitoring and evaluating the activities included in the study. The findings from this study encourage the use of microcomputers and MIS for efficient monitoring and evaluation of the entire activities of PHC programs. Details will be discussed and illustrations presented.

COMPUTERIZATION OF PRIMARY HEALTH CARE: THINKING ABOUT THE FUTURE, FM Felimban, King Saud University Medical College, Department of Family & Community Medicine, Riyadh

The provision of comprehensive continuous care is an important strategy of PHC services. The availability and accessibility to a well-constructed data base and a method for its collection and recording will help to achieve such an aim. Information in a manual system—currently in use—is passive, requires human effort to retrieve and collate, and may inhibit attempts at cross referencing. In comparison, the ability to store, retrieve, sort, analyze, compile, report, and integrate large amounts of data makes the computer an interesting and imperative technology for PHC professionals. Moreover, computerization of PHC files enables individuals to have their personal medical identification code with them at all times, which is of a great benefit if they become ill when away from their usual source of care or if they are unable to provide information because of severe illness or injury. At this stage of our PHCC development, the time has come to think about the potential roles of such technology in organizing center services, aid communication, and optimize population care. The present paper highlights the emerging concept of computerization in PHCCs and provides an approach to computer application in improving PHCC information systems. The future pattern of a national computing organization can be started at regional levels, which later can be linked to a central computer system and expanded to local areas according to the financial resources devoted to such a project. The computerization of PHC files for national use may require a specific coding system that should be *standardized* all over the Kingdom and the development of a *national standard mainframe system* can facilitate the implementation of an economic and effective computer system in the Saudi PHCC network and support the maintenance and operational procedures.

ANTENATAL CARE USING A HIGH-RISK SCORING SHEET BY SAUDI HEALTH VISITORS IN QATEEF AREA, EASTERN PROVINCE, GM Al-Qatari, K Al-Awwami, M Al-Youif, A Al-Mubarik, D Al-Nasir, K Al-Rabaan, Primary Health Care Department, Qateef.

The screening of pregnant women to identify factors likely to result in complicated pregnancy and/or delivery is recognized, with variable types of high-risk scoring systems used by different levels of health workers, ranging from Ob/Gyn Specialists to health workers with short training experiences. Our paper describes an MCH training program that has been in existence for the last four years. The program trains newly graduated Saudi nurses for three full months on MCH activities, including home and school visits. One of the activities they are trained to do is using a high-risk scoring sheet that has been devised with the help of the Ob/Gyn Department at Qateef Central Hospital. The high-risk scoring sheet was described and the high-risk factors detected at various health centers were analyzed and discussed, taking into consideration the results of similar programs in the Kingdom and abroad with the aim of assessing the quality of antenatal care delivered by our health visitors.

REVIEW OF PRIMARY HEALTH CARE AT THE COMMUNITY LEVEL IN GIZAN, MK Goyal, AM Amin, AR Ageel, Department of Preventive Medicine, Directorate General of Health, MOH, Gizan

Gizan, in the southwest province of the Kingdom of Saudi Arabia, has made remarkable progress in implementing primary health care, toward achievement of the goal "health for all." The coverage for immunization and some other aspects of primary health care has been studied in the past. The present study was planned with the aim of obtaining baseline data about the health status of people in relation to their living environment and utilization of health services. The cluster sample technique was used to examine the rural and urban population. Immunization status of 600 children (aged 12-23 months) was evaluated to calculate the coverage by vaccines and their doses. Mothers were interviewed concerning their knowledge and practice of maternity and child health care. The findings have been analyzed and compared with some previous reports after studies at the national and regional level. Some important observations have been made regarding the availability of preventive and promotive services in all health centers, moderately high coverage by EPI vaccines, significantly high antenatal booking among expectant mothers, good knowledge by a sizable number of mothers about oral rehydration treatment, etc. Some problems and deficiencies have also been identified and corrective measures suggested.

Announcements

The *Annals of Saudi Medicine* is pleased to publish announcements of educational opportunities of interest to its readers. For adequate publicity, notices of postgraduate courses, meetings, and lectures must be received at least 6 months before the date of occurrence. Please send relevant information to the *Annals of Saudi Medicine*, Publications Office, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia.

King Saud University Fellowship in Pathology

King Saud University announces the inception of a 5-year joint fellowship training program in pathology. The training will be at King Khalid University Hospital, King Faisal Specialist Hospital and Research Centre, and Riyadh Armed Forces Hospital, and is a full-time program. Application is open to interested and suitably qualified residents from all over the Kingdom. To be eligible, applicants will meet the following criteria:

1. Doctors who hold MB,BS from King Saud University or equivalent degree with at least Good grade.
2. Doctors who have finished their internship in a recognized hospital with at least a Very Good grade.
3. Successful completion of a selection examination and personal interview.
4. Applicants from other institutions should submit a letter from his/her employer that he/she will be sponsored during the whole period of training.

Applications and inquiries should be sent to the Director, Postgraduate Medical Education, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia.

King Faisal Specialist Hospital and Research Centre Postgraduate Training Programs

King Faisal Specialist Hospital and Research Centre is pleased to invite applications for the following full-time postgraduate training programs:

1. Arab Board residency training in the specialties of internal medicine, obstetrics/gynecology, pediatrics, and surgery.
2. Five-year pathology residency training program, affiliated with the Royal College of Pathologists of Australasia and the King Saud University.
3. Fellowships, both adult and pediatric, in cardiology, endocrinology, gastroenterology, infectious diseases, nephrology, hematology, and oncology. Also, adult pulmonary and critical care medicine, adult rheumatology, pediatric allergy and clinical immunology, neonatal/perinatal medicine, and pediatric neurology.

For further information contact the Director, Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia; telephone (01) 464-7272, extension 1837.

Symposium on Modern Trends in Transfusion Medicine

A symposium on Modern Trends in Transfusion Medicine will be held at King Fahd Hospital of King Faisal University, Al-Khobar, Saudi Arabia, on December 6, 1990. The program is intended to cover all clinical aspects of transfusion medicine, including autotransfusion, HIV transmission, blood substitutes, hemostatic drugs, and topical agents. Abstracts must be received by 8 October 1990, and should be addressed to: Dr. Majed Al-Awami, P.O.Box 2931, Al-Khobar 31952; telephone 898-4317; fax 864-5927; telex 670277 KOHOSP SJ. For information regarding the meeting, contact: Prof. M.S.Khwaja, Coordinator of CME in Surgery, Department of Surgery, King Fahd Hospital of the University, Al-Khobar 31952.

Radiopharmaceuticals from King Faisal Specialist Hospital and Research Centre

King Faisal Specialist Hospital and Research Centre manufactures various radiopharmaceuticals at its Radionuclide and Cyclotron Operations facility with the aid of model CS-30 Cyclotron. These radiopharmaceuticals are produced according to international standards of good manufacturing practice. The Research Centre meets the high standards of quality assurance and environmental safety with regard to radiopharmaceuticals.

Radiopharmaceuticals currently produced and available for distribution throughout the Kingdom and to adjoining Arab states are as follows: thallous (T1-201) chloride injection ($T^{1/2}$ = 73 h); gallium (Ga-67) citrate injection ($T^{1/2}$ = 78.3 h); iodine-123 capsules ($T^{1/2}$ = 13.1 h); iodine-123 oral solution ($T^{1/2}$ = 13.1 h); iodine-123 orthoiodohippurate solution ($T^{1/2}$ = 13.1 h); rubidium (Rb-81) → krypton (Kr-81 m) generator ($T^{1/2}$ = 4.58 h – 13 s); indium (In-111) oxine ($T^{1/2}$ = 67.92 h) for cell labeling; indium (In-111) DTPA for cisternography ($T^{1/2}$ = 67.92 h).

Suggestions from the medical community for additional cyclotron-produced needs are welcome.

Inquiries concerning the availability, price schedule; and technical information on specific radiopharmaceuticals should be directed to: Abbass H. Al-Marzouky, MD, Executive Director, Research Centre, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia (Fax No. 966-1-441-4839).

Call for abstracts: Fourth Scientific Session, Saudi Heart Association

Abstracts for presentation are being accepted for the Fourth Scientific Session of the Saudi Heart Association to be held in Riyadh, Saudi Arabia, on 28–30 Rajab 1411H (12–14 February 1991). Original works related to all aspects of cardiovascular diseases will be considered, with particular emphasis on: (1) coronary artery disease; (2) valvular heart disease; (3) pericardial disease; (4) interventional cardiology; (5) noninvasive cardiology; (6) infective endocarditis; (7) cardiac surgery; (8) pediatric cardiology; and (9) cardiac anesthesia.

Abstracts submitted for consideration must be received by the organizing committee no later than 15 Safar 1411H (15 September 1990). Further information regarding submission of abstracts may be obtained from the Saudi Heart Association, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia: telephone (01) 467-1556 or 567-1554.

Symposium on Upper Gastrointestinal Bleeding, King Fahd Hospital

A symposium on upper gastrointestinal bleeding and its management will be held on Thursday, 8 November 1990; at King Fahd Hospital of King Faisal University, Al-Khobar. This program will focus on important aspects of portal hypertension and peptic ulcer disease. For information contact: Dr. Abdul Aziz Al-Quorain, P.O.Box 40001, Al-Khobar 39152, Saudi Arabia: telephone 898-3931; fax 864-5927.

Joint Board for Postgraduate Medical Education Symposia for 1411

The Joint Board for Postgraduate Education is pleased to announce the following symposia for 1411.

1. Geriatrics and Geriatric Rehabilitation Symposium; Riyadh Central Hospital, 24-25 Rabi Al-Thani 1411 (11-12 November 1990).
2. 8th Saudi Annual Neurosciences Symposium; King Faisal Specialist Hospital and Research Centre, 27-29 Jumada Al-Thani 1411 (13-15 January 1991).
3. 6th Annual Paediatric Symposium; College of Medicine, King Saud University, 26-27 Rajab 1411 (10-11 February 1991).
4. 4th Saudi Gastroenterology and Hepatology Symposium; Security Forces Hospital, 10-12 Shaban 1411 (24-26 February 1991).
5. Advances in Thrombosis Management Symposium; Riyadh Central Hospital, 17-18 Shaban 1411 (3-4 March 1991).
6. Postgraduate and Continuing Medical Education; College of Medicine, King Saud University, 21-22 Shawwal 1411 (5-6 May 1991).

For further information, contact the Joint Board Office, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia; telephone (01) 467-1556 or 1564; telefax 481-1853; telex 403748 DARAYAH SJ.

The 10th Overseas Medical Conference

The Arab Medical Association (AAMA) in collaboration with the Joint Board for Postgraduate Education and Security Forces Hospital announce the 10th Overseas Medical Conference to be held at Security Forces Hospital, Riyadh, from 12 to 15 Jumada Al-Thani 1411 (29 December 1990 to 1 January 1991). As many as fifty international speakers will be participating, as well as prominent local speakers. The main topics for presentation will cover surgery, medicine, pediatrics, and obstetrics and gynecology. For information, contact: Joint Board Office, Postgraduate Centre, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia.

King Faisal Specialist Hospital and Research Centre Symposia for 1411

King Faisal Specialist Hospital and Research Centre is pleased to announce the following educational activities for 1411.

1. Pediatric and Adult Allergy Workshop; 19 Rabi Al Thani 1411 (6 November 1990)
2. Orthopedic Review Course; 15–18 Jumada Al Awal 1411 (2–5 December 1990)
3. First International Workshop on IVF in the Middle East; 28 Jumada Al Awal–1 Jumada Al Thani 1411 (15–18 December 1990)
4. Symposium on Infertility; 2 Jumada Al Thani 1411 (19 December 1990)
5. Gamma Knife Workshop; King Faisal Specialist Hospital and Research Centre, 24 Jumada Al-Thani 1411 (12 January 1991).
6. 8th Annual Neurosciences Symposium;* 27–29 Jumada Al Thani 1411 (13–15 January 1991)
7. FMGEMS Examination; 7–8 Rajab 1411 (22–23 January 1991)
8. Heart Valve Reconstruction Symposium; 14–16 Rajab 1411 (29–31 January 1991)
9. Symposium on Therapy of Parasitic Diseases: Advances and Problems; 28–29 Rajab 1411 (12–13 February 1991)
10. Molecular Biology of Cancer Symposium; 11–13 Shaban 1411 (25–27 February 1991)
11. FMGEMS Examination; 12–13 Muharram 1412 (23–24 July 1991)

For further information, contact Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211; telephone 464-7272, extension 1865 or 1834, fax 442-7237.

*Sponsored by the Joint Board for Postgraduate Medical Education.

Chinese University of Hong Kong, Third International Imaging Course

The Third International Imaging Course (35 hours of Category I accreditation) will be held from 29 October to 4 November, 1990, at the Regal Riverside Hotel, Shatin, Hong Kong. Course directors are: Professors L.Kreel, C. Metreweli, and T.L. Lawson. For further information, please contact: Miss Rebecca Tsui, Department of Radiology, Prince of Wales Hospital, Shatin, Hong Kong. Tel.: 636 3213; Fax.: 636 0012.

The Arab American Medical Association (AAMA)
In collaboration with
The Joint Board for Postgraduate Medical Education,
Security Forces Hospital, M.S.D.,
& Ministry of Interior, Riyadh
announces

THE TENTH OVERSEAS MEDICAL CONFERENCE
Riyadh, Saudi Arabia

to be held at
SECURITY FORCES HOSPITAL, RIYADH

12 – 15 Jumada Thani 1411
29 December 1990 – 1 January 1991

Abstracts are invited for selection and should be submitted before:
8 Dhulqada 1410 (1 June 1990)

Abstracts should be related to the following topics:
(Papers,.Videos, Cinni or Poster presentation)

SURGERY

Recent advances in the management of:
Cholithiasis, Urolithiasis, Portal Hypertension,
Morbid Obesity, Carcinoma of Prostate, Urinary Tract Infection,
Male Infertility and Impotence

Recent advances in:
Organ Transplant, Paediatric Surgery, Mesenteric Vascular Accident,
Use of Laser and Tumour Markers, Therapeutic Gastrointestinal Endoscopy,
Limb Equalising Procedures, Joint Arthroplasty,
Diagnostic and Therapeutic Arthroscopy, Management of Painful Shoulder,
Management of Resistant Cases of Rheumatoid Arthritis

MEDICINE

Pathogenesis and Therapeutic Approach to Coronary Artery Disease,
Thrombolytic Therapy, Infective Endocarditis,
Hepatology: Cirrhosis/Hepatitis/Cancer follow-up,
Management of Brucellosis, Immunology: SLE/AIDS/Vasculitis,
Molecular and RBC Genetic Abnormalities,
Current Concepts in the Management of Hyperlipidemia

PAEDIATRICS

Spectrum of Chronic Renal Failure in Children, Failure to Thrive: New Outlook,
Burkitt's Lymphoma and Hodgkin's Disease, Ricketts and Osteomalacia,
Lead Poisoning, Nutrition and Metabolic Disorders

OBSTETRICS and GYNAECOLOGY

Early Wastage of Pregnancy, Foetal Monitoring: High Risk Pregnancy,
Urological Complications in Obstetrics and Gynaecology, Use of Ultrasound,
Prostaglandin Use in Obstetrics and Gynaecology,
Diseases in Pregnancy, Female Infertility

GENERAL TOPICS

Medical Education, Scope of Primary Health Care, Advances in Medical Technology

REGISTRATION

Pre-Registration is Required

ABSTRACT GUIDELINES

Abstracts should not exceed more than 250 words
Indicate presenting author
Indicate audiovisual aid required
(Slide projector I or II, Video-Betamax or VHS, Cinni projection)

Abstracts should be addressed to:

Chairman of the Scientific Committee
The 10th Overseas Medical Conference (AAMA)
The Joint Board for Postgraduate Medical Education
College of Medicine, King Saud University
P.O. Box 2925, Riyadh 11461
Saudi Arabia

CONTACT

The Joint Board for Postgraduate Medical Education
College of Medicine, King Saud University
P.O. Box 2925, Riyadh 11461
Saudi Arabia
Tel: 467-1551/1556/1564
Fax: 481-1853

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الجمعية الطبية العربية الامريكية
بالتعاون
مع المجلس المشترك للدراسات الطبية العليا
ومستشفى قوى الأمن
الادارة العامة للخدمات الطبية
وزارة الداخلية ـ المملكة العربية السعودية

المؤتمر الطبي السنوي العاشر خارج الولايات المتحدة
المملكة العربية السعودية • الرياض

يعقـد فـي:
مستشفى قـوى الأمـن ـ الرياض
السبت ـ الثـلاثـاء
١٢ ـ ١٥ جمادى الآخرة ١٤١١هـ/ ٢٩ ديسمبر ١٩٩٠ ـ ١ يناير ١٩٩١م
آخر موعد لقبول ملخص الابحاث هو:
٨ ذو القعدة ١٤١٠هـ [١ يونيو ١٩٩٠م]
على أن يكون موضوع الابحاث المقدمة الموضوعات التالية:
[ابحـاث، افـلام طبية او ملصقـات]

الجـــراحـــة

احدث التطورات في الأساليب العلاجية في مجال:
داء الحصوات الصفراوي، وداء الحصوات البولي، فرط ضغط الدم البابي، السمنة المرضية، سرطان غدة البروستات، إلتهاب المسالك البولية، العقم عند الذكور، والعنانة

احدث الأساليب في مجال:
جراحة زراعة الاعضاء، جراحة الأطفال، الحوادث المساريقية الوعائية، استخدام الليزر في مؤشرات الأورام، التنظير الداخلي العلاجي للجهاز الهضمي، عمليات تسوية الأطراف واستبدال المفاصل، تنظير المفصل التشخيصي والعلاجي، اساليب معالجة علاج الكتف المؤلمة، أساليب معالجة حالات التهاب المفاصل الرثوي [الروماتزمي] المقاوم

الأمـراض الباطنـة:

نشوء وعلاج امراض قصور الشريان التاجي، علاج انحلال الخثرة، إلتهاب الشغاف الانتاني علم الكبد: التليف (التشمع)، إلتهاب الكبد، متابعة السرطان، اساليب علاج داء الحمى المالطية

المنـاعـة: داء الذئبة الحمامية، فقدان المناعة المكتسبة، التهاب الأوعية الدموية، الشذوذ الجزيئي والوراثي لخلايا الدم الحمراء، المفاهيم المعاصرة في علاج فرط تدسم الدم

طب الأطفال:

الفشل الكلوي المزمن عند الأطفال، تأخر نمو الأطفال، مرض بيركت، ومرض هدجكن، كساح الأطفال وتلين العظام، التسمم الرصاصي، الاضطرابات الإستقلابية والغذائية

امـراض النساء والولادة:

الفقد المبكر للحمل، مراقبة نمو الجنين، الحمل ذو المخاطر الكبيرة، مضاعفات المسالك البولية في أمراض النساء والولادة، استخدامات الأشعة فوق الصوتية، استعمال البروستغلندين في علاج أمراض النساء والولادة، أمراض فترة الحمل، العقم عند النساء

مـوضـوعـات عـامـة:

التعليم الطبي، مجالات الرعاية الصحية الأولية، أحدث التطورات في التقنية الطبية

التسجيـــل: التسجيل المسبق ضروري

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- تحديد وسائل الإيضاح المطلوبة [جهاز فيديو بتاماكس، في إتش إس، جهاز عرض شرائح]

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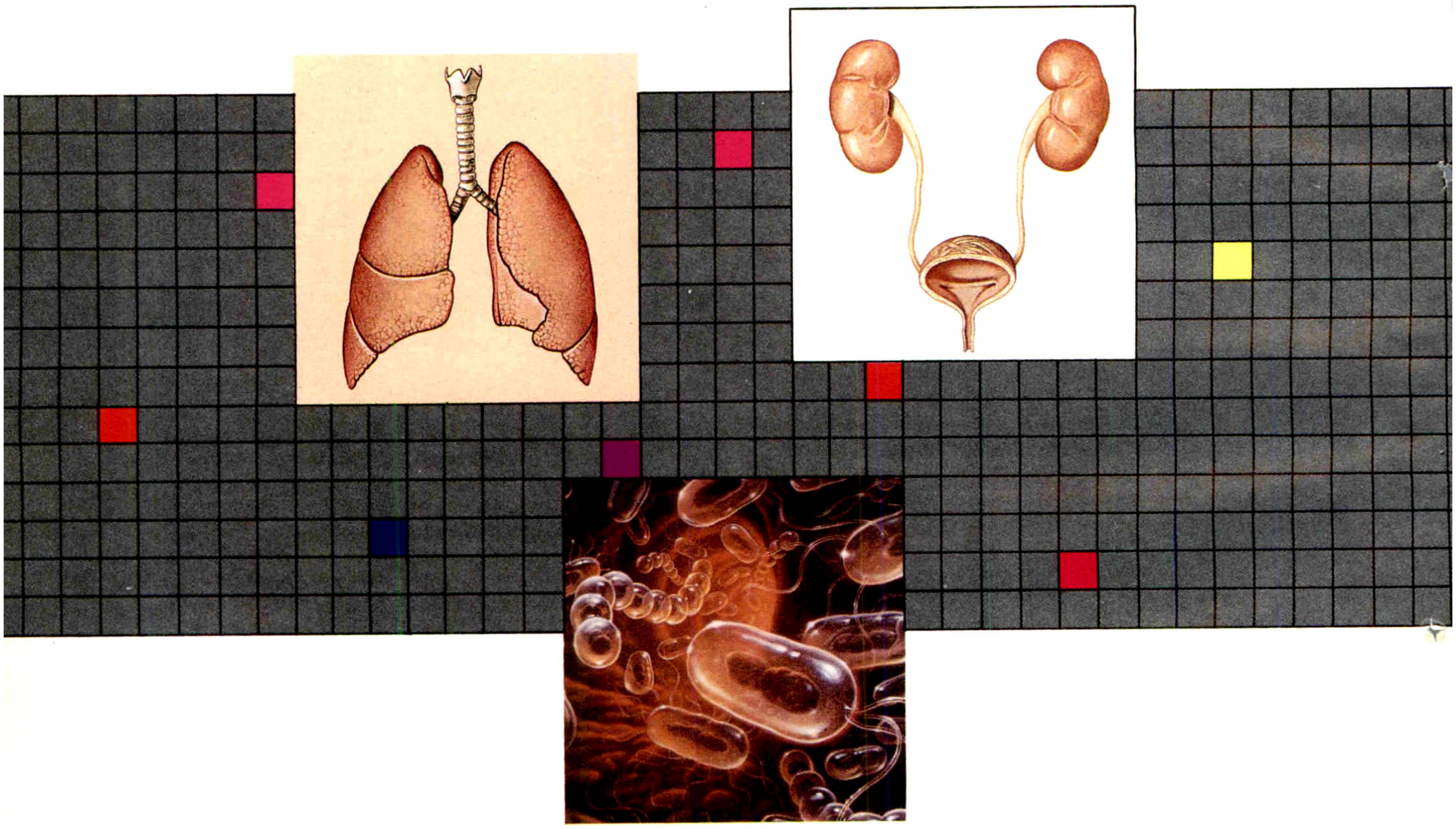

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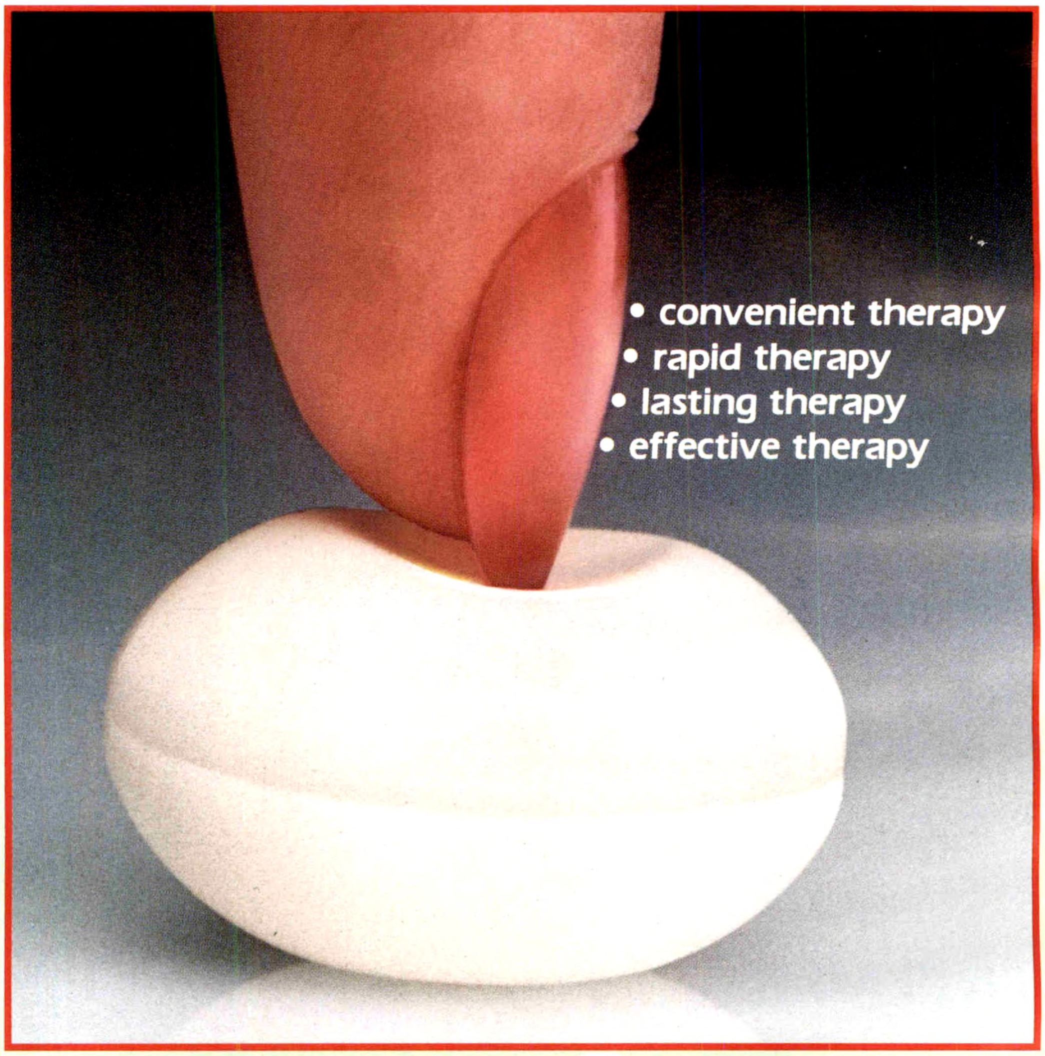

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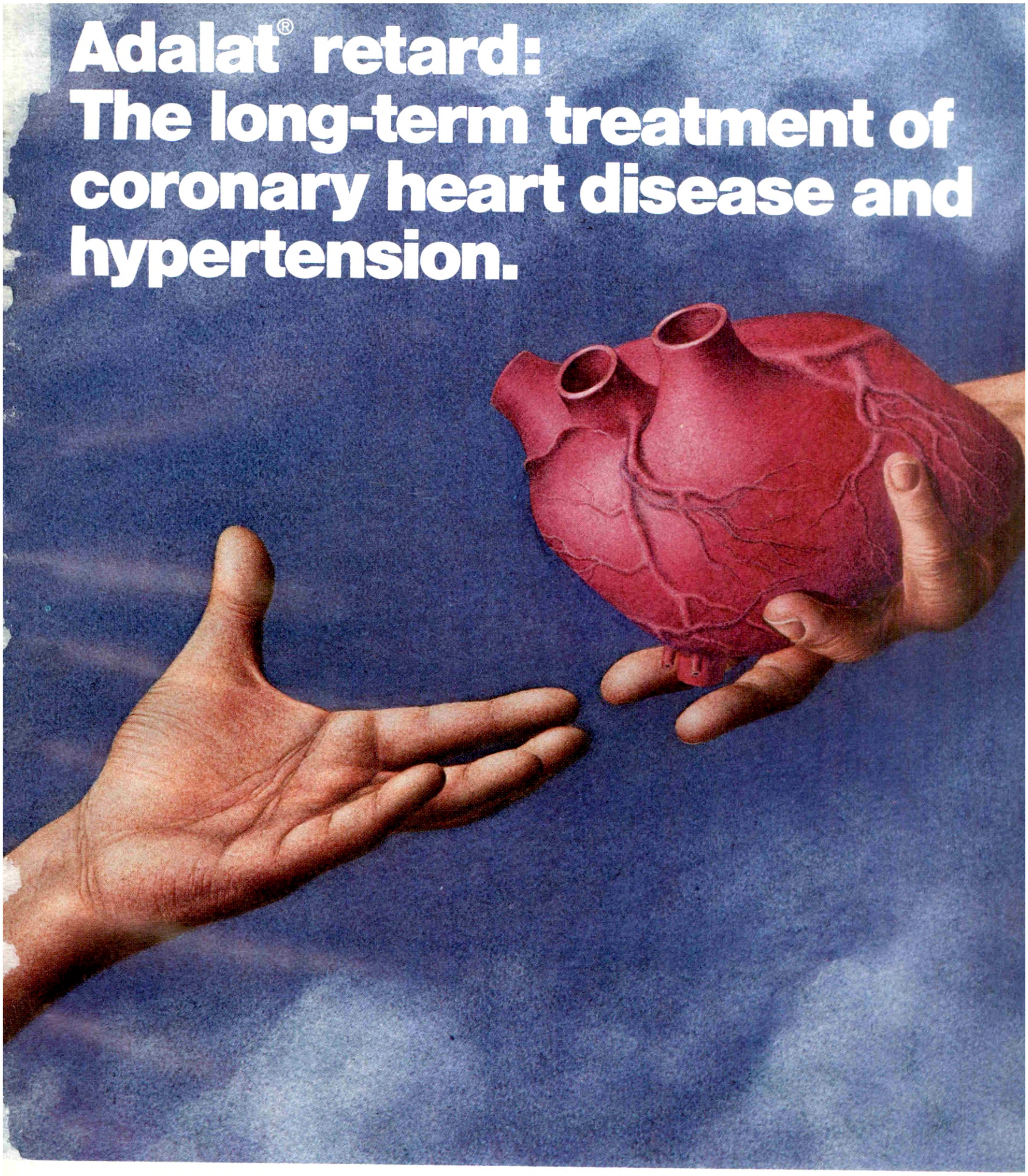
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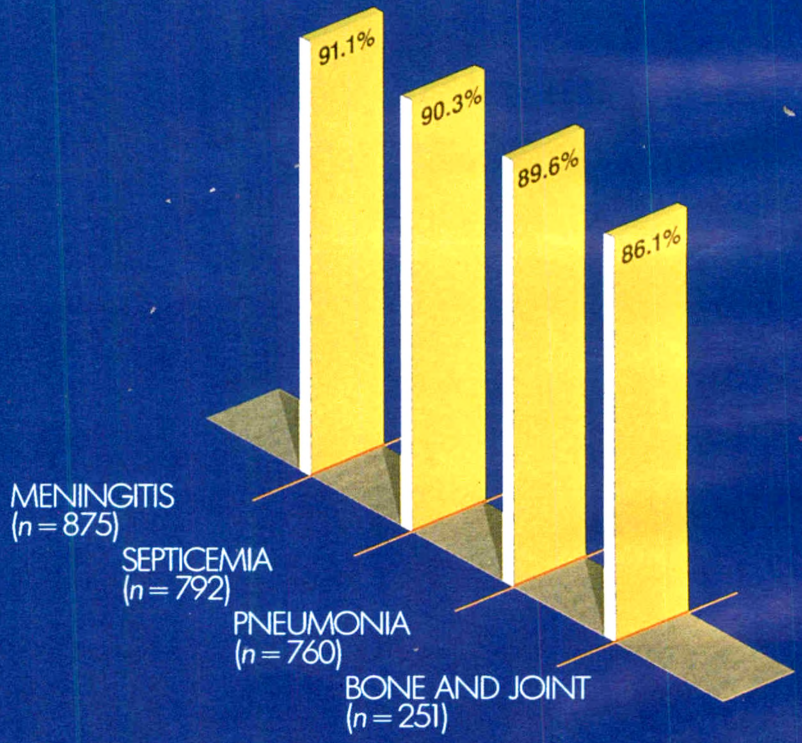

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Reference: Data on file, F. Hoffmann-La Roche Ltd, Basel, Switzerland

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المجلد ١٠ العدد ٥ صفر ١٤١١هـ سبتمبر ١٩٩٠م

المدونات الطبية السعودية

هيئة التحرير

رئيس التحرير الدكتور بيتر بي هيردسون

الدكتور محمد أختر
الدكتور ماجد عامر
الدكتور كارلوس دوران
الدكتور صلاح الفقيه
الدكتور محمد زهير القاوي

الدكتور عبدالعزيز المشاري
الدكتور منصور النزهة
الدكتور خالد طبارة
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رئيس التحرير: الدكتور بيتر بي هيردسون
المحرر الإداري: الدكتور سعدي طاهر
محرر النصوص العربية: الدكتور محمد زهير القاوي
محرر فني: بتي ب لانج
مساعدة محرر فني: ماري آن دي سانتس

مساعدتا التحرير:
فرجينيا جي كروزير
شيرلي موفيت

المدونات الطبية السعودية مجلة تنشر بموجب الأمر الملكي السامي رقم ٥/م/٢٤٢٢٣ بتاريخ ١٤ شوال عام ١٤٠٠هـ. وتصدر مرة كل شهرين، وهي مشروع مشترك بين كل من كلية الطب ومستشفى الملك خالد الجامعي ـ جامعة الملك سعود، صندوق بريد ٢٩٢٥ ـ الرياض ١١٤٦١، المملكة العربية السعودية، ومستشفى الملك فيصل التخصصي ومركز الأبحاث، صندوق بريد ٣٣٥٤ ـ الرياض ١١٢١١، المملكة العربية السعودية. يتم صف وطبع المجلة بمطابع جامعة الملك سعود. يتم توزيع المدوَّنات بواسطة قسم البريد التابع لإدارة الخدمات الإدارية بمستشفى الملك فيصل التخصصي ومركز الأبحاث. كما يتولى قسم الترجمة في هذه الإدارة إعداد الملخصات العربية بالاشتراك مع الدكتور محمد زهير القاوي. كل المراسلات والاستفسارات وطرق الحصول على المستلات ترسل إلى مكتب المطبوعات على العنوان التالي:

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مدونات الطب السعودي
مستشفى الملك فيصل التخصصي ومركز الأبحاث
ص. ب ٣٣٥٤
الرياض ١١٢١١ ـ المملكة العربية السعودية

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BACTROBAN is a product of research from Beecham Pharmaceuticals, Brentford, England. BACTROBAN is a trademark.

References: 1. Wainscott G. *R Soc Med Int Cong and Symp Series 80:* 173. 2. Cockburn A et al. *Excerpta Medica Curr Clin Pract Ser* 1985; 16: 11. 3. White DG et al. *J. Infect* 1989; 18: 221. 4. Kennedy CTC et al. *R. Soc Med Int Cong Symp Ser* 1984; (80): 79. 5. Gratton D. *Int J Dermatol* 1987; 26(7): 472. 6. Maddin S et al. *Proc 6th Mediterr Congr Chemother Taormina* 1988; Abstract 471.

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